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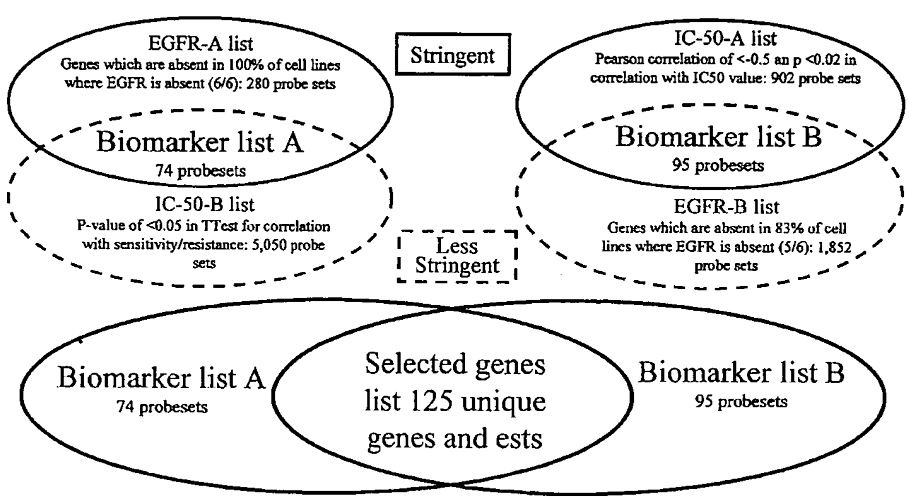
(54) Title: BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS



(57) Abstract: EGFR biomakers useful in a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises (a) exposing the mammal to the EGFR modulator and (b) measuring in the mammal level of at least one biomaker, wherein a difference in the level in at least one biomaker measured in (b) compared to the level of the biomaker in a mammal that has not been exposed to the EGFR modulator indicates that the mammal will respond therapeutically to the method of treating cancer.

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BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS

FIELD OF THE INVENTION

The present invention relates generally to the field of pharmacogenomics, and more specifically to methods and procedures to determine sensitivity in patients to allow the development of individualized genetic profiles which aid in treating diseases and disorders based on patient response at a molecular level.

BACKGROUND OF THE INVENTION:

Cancer is a disease with extensive histoclinical heterogeneity. Although conventional histological and clinical features have been correlated to prognosis, the same apparent prognostic type of tumors varies widely in its responsiveness to therapy and consequent survival of the patient.

New prognostic and predictive markers, which would facilitate an individualization of therapy for each patient, are needed to accurately predict patient response to treatments, such as small molecule or biological molecule drugs, in the clinic. The problem may be solved by the identification of new parameters that could better predict the patient's sensitivity to treatment. The classification of patient samples is a crucial aspect of cancer diagnosis and treatment. The association of a patient's response to a treatment with molecular and genetic markers can open up new opportunities for treatment development in non-responding patients, or distinguish a treatment's indication among other treatment choices because of higher confidence in the efficacy. Further, the pre-selection of patients who are likely to respond well to a medicine, drug, or combination therapy may reduce the number of patients needed in a clinical study or accelerate the time needed to complete a clinical development program (M. Cockett et al., 2000, *Current Opinion in Biotechnology*, 11:602-609).

The ability to predict drug sensitivity in patients is particularly challenging because drug responses reflect not only properties intrinsic to the target cells, but also a host's metabolic properties. Efforts to use genetic information to predict drug sensitivity have primarily focused on individual genes that have broad effects, such as the multidrug resistance genes, *mdr1* and *mrp1* (P. Sonneveld, 2000, *J. Intern. Med.*, 247:521-534).

The development of microarray technologies for large scale characterization of gene mRNA expression pattern has made it possible to systematically search for molecular markers and to categorize cancers into distinct subgroups not evident by traditional histopathological methods (J. Khan et al., 1998, *Cancer Res.*, 58:5009-5013; A.A. Alizadeh et al., 2000, *Nature*, 403:503-511; M. Bittner et al., 2000, *Nature*, 406:536-540; J. Khan et al., 2001, *Nature Medicine*, 7(6):673-679; and T.R. Golub et al., 1999, *Science*, 286:531-537; U. Alon et al., 1999, *Proc. Natl. Acad. Sci. USA*, 96:6745-6750). Such technologies and molecular tools have made it possible to monitor the expression level of a large number of transcripts within a cell population at any given time (see, e.g., Schena et al., 1995, *Science*, 270:467-470; Lockhart et al., 1996, *Nature Biotechnology*, 14:1675-1680; Blanchard et al., 1996, *Nature Biotechnology*, 14:1649; U.S. Patent No. 5,569,588 to Ashby et al.).

Recent studies demonstrate that gene expression information generated by microarray analysis of human tumors can predict clinical outcome (L.J. van't Veer et al., 2002, *Nature*, 415:530-536; M. West et al., 2001, *Proc. Natl. Acad. Sci. USA*, 98:11462-11467; T. Sorlie et al., 2001, *Proc. Natl. Acad. Sci. USA*, 98:10869-10874; M. Shipp et al., 2002, *Nature Medicine*, 8(1):68-74). These findings bring hope that cancer treatment will be vastly improved by better predicting the response of individual tumors to therapy.

Needed are new and alternative methods and procedures to determine drug sensitivity in patients to allow the development of individualized genetic profiles which are necessary to treat diseases and disorders based on patient response at a molecular level.

SUMMARY OF THE INVENTION:

The invention provides methods and procedures for determining patient sensitivity to one or more Epidermal Growth Factor Receptor (EGFR) modulators. The invention also provides methods of determining or predicting whether an individual requiring therapy for a disease state such as cancer will or will not respond to treatment, prior to administration of the treatment, wherein the treatment comprises one or more EGFR modulators. The one or more EGFR modulators are compounds that can be selected from, for example, one or more EGFR specific ligands, one or

more small molecule EGFR inhibitors, or one or more EGFR binding monoclonal antibodies.

In one aspect, the invention provides a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4; (b) exposing the mammal to the EGFR modulator; (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker, wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

As used herein, respond therapeutically refers to the alleviation or abrogation of the cancer. This means that the life expectancy of an individual affected with the cancer will be increased or that one or more of the symptoms of the cancer will be reduced or ameliorated. The term encompasses a reduction in cancerous cell growth or tumor volume. Whether a mammal responds therapeutically can be measured by many methods well known in the art, such as PET imaging.

The at least one biomarker can also be selected from the biomarkers of Table 5. The mammal can be, for example, a human, rat, mouse, dog rabbit, pig sheep, cow, horse, cat, primate, or monkey.

The method of the invention can be, for example, an in vitro method and wherein the at least one biomarker is measured in at least one mammalian biological sample from the mammal. The biological sample can comprise, for example, at least one of whole fresh blood, peripheral blood mononuclear cells, frozen whole blood, fresh plasma, frozen plasma, urine, saliva, skin, hair follicle, or tumor tissue.

In another aspect, the invention provides a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) exposing the mammal to the EGFR modulator; (b) following the exposing of step (a), measuring in the mammal the level of the at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of the at least one biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been

exposed to said EGFR modulator, indicates that the mammal will respond therapeutically to said method of treating cancer.

In yet another aspect, the invention provides a method for testing or predicting whether a mammal will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises: (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4; (b) exposing the mammal to the EGFR modulator; (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker, wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

In another aspect, the invention provides a method for determining whether a compound inhibits EGFR activity in a mammal, comprising: (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the compound inhibits EGFR activity in the mammal.

In yet another aspect, the invention provides a method for determining whether a mammal has been exposed to a compound that inhibits EGFR activity, comprising (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the mammal has been exposed to a compound that inhibits EGFR activity.

In another aspect, the invention provides a method for determining whether a mammal is responding to a compound that inhibits EGFR activity, comprising (a) exposing the mammal to the compound; and (b) following the exposing of step (a), measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, wherein a difference in the level of said biomarker measured

in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said compound, indicates that the mammal is responding to the compound that inhibits EGFR activity.

As used herein, "responding" encompasses responding by way of a biological and cellular response, as well as a clinical response (such as improved symptoms, a therapeutic effect, or an adverse event), in a mammal

The invention also provides an isolated biomarker selected from the biomarkers of Table 4. The biomarkers of the invention comprise sequences selected from the nucleotide and amino acid sequences provided in Table 4 and the Sequence Listing, as well as fragments and variants thereof.

The invention also provides a biomarker set comprising two or more biomarkers selected from the biomarkers of Table 4.

The invention also provides kits for determining or predicting whether a patient would be susceptible or resistant to a treatment that comprises one or more EGFR modulators. The patient may have a cancer or tumor such as, for example, a colon cancer or tumor.

In one aspect, the kit comprises a suitable container that comprises one or more specialized microarrays of the invention, one or more EGFR modulators for use in testing cells from patient tissue specimens or patient samples, and instructions for use. The kit may further comprise reagents or materials for monitoring the expression of a biomarker set at the level of mRNA or protein.

In another aspect, the invention provides a kit comprising two or more biomarkers selected from the biomarkers of Table 4.

In yet another aspect, the invention provides a kit comprising at least one of an antibody and a nucleic acid for detecting the presence of at least one of the biomarkers selected from the biomarkers of Table 4. In one aspect, the kit further comprises instructions for determining whether or not a mammal will respond therapeutically to a method of treating cancer comprising administering a compound that inhibits EGFR activity. In another aspect, the instructions comprise the steps of (a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4, (b) exposing the mammal to the compound, (c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker,

wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

The invention also provides screening assays for determining if a patient will be susceptible or resistant to treatment with one or more EGFR modulators.

The invention also provides a method of monitoring the treatment of a patient having a disease treatable by one or more EGFR modulators.

The invention also provides individualized genetic profiles which are necessary to treat diseases and disorders based on patient response at a molecular level.

The invention also provides specialized microarrays, e.g., oligonucleotide microarrays or cDNA microarrays, comprising one or more biomarkers having expression profiles that correlate with either sensitivity or resistance to one or more EGFR modulators.

The invention also provides antibodies, including polyclonal or monoclonal, directed against one or more biomarkers of the invention.

The invention will be better understood upon a reading of the detailed description of the invention when considered in connection with the accompanying figures.

BRIEF DESCRIPTION OF THE FIGURES:

FIG. 1 illustrates a EGFR biomarker identification and prioritization strategy.

FIG. 2A illustrates the RT-PCR results for EGFR in thirty one colon cancer cell lines to identify cell lines which do not have significant mRNA expression of EGFR.

FIG. 2B illustrates the IC_{50} profile for twenty two colon cancer cell lines with an EGFR inhibitor compound, and determination of sensitive and resistant cell lines.

DETAILED DESCRIPTION OF THE INVENTION:

The invention provides biomarkers that respond to the modulation of a specific signal transduction pathway and also correlate with EGFR modulator sensitivity or resistance. These biomarkers can be employed for predicting response to one or more EGFR modulators. In one aspect, the biomarkers of the invention are those provided in Table 4 and the Sequence Listing, including both polynucleotide and polypeptide sequences.

The biomarkers were determined by an *in vitro* assay employing microarray technology to monitor simultaneously the expression pattern of thousands of discrete genes in untreated cells, whose response to the modulation of a signal transduction pathway, in particular the EGFR pathway, was tested on untreated cells whose sensitivity to EGFR modulators was tested. The biomarkers have expression levels in the cells that are dependent on the activity of the EFGR signal transduction pathway and that are also highly correlated with EGFR modulator sensitivity exhibited by the cells. Biomarkers serve as useful molecular tools for predicting a response to EGFR modulators, preferably biological molecules, small molecules, and the like that affect EGFR kinase activity via direct or indirect inhibition or antagonism of EGFR kinase function or activity.

EGFR MODULATORS

As used herein, the term "EGFR modulator" is intended to mean a compound or drug that is a biological molecule or a small molecule that directly or indirectly modulates EGFR activity or the EGFR signal transduction pathway. Thus, compounds or drugs as used herein is intended to include both small molecules and biological molecules. Direct or indirect modulation includes activation or inhibition of EGFR activity or the EGFR signal transduction pathway. In one aspect, inhibition refers to inhibition of the binding of EGFR to an EGFR ligand such as, for example, EGF. In another aspect, inhibition refers to inhibition of the kinase activity of EGFR.

EGFR modulators include, for example, EGFR specific ligands, small molecule EGFR inhibitors, and EGFR monoclonal antibodies. In one aspect, the EGFR modulator inhibits EGFR activity and/or inhibits the EGFR signal transduction

pathway. In another aspect, the EGFR modulator is an EGFR antibody that inhibits EGFR activity and/or inhibits the EGFR signal transduction pathway.

EGFR modulators include biological molecules or small molecules. Biological molecules include all lipids and polymers of monosaccharides, amino acids, and nucleotides having a molecular weight greater than 450. Thus, biological molecules include, for example, oligosaccharides and polysaccharides; oligopeptides, polypeptides, peptides, and proteins; and oligonucleotides and polynucleotides. Oligonucleotides and polynucleotides include, for example, DNA and RNA.

Biological molecules further include derivatives of any of the molecules described above. For example, derivatives of biological molecules include lipid and glycosylation derivatives of oligopeptides, polypeptides, peptides, and proteins.

Derivatives of biological molecules further include lipid derivatives of oligosaccharides and polysaccharides, e.g., lipopolysaccharides. Most typically, biological molecules are antibodies, or functional equivalents of antibodies. Functional equivalents of antibodies have binding characteristics comparable to those of antibodies, and inhibit the growth of cells that express EGFR. Such functional equivalents include, for example, chimerized, humanized, and single chain antibodies as well as fragments thereof.

Functional equivalents of antibodies also include polypeptides with amino acid sequences substantially the same as the amino acid sequence of the variable or hypervariable regions of the antibodies. An amino acid sequence that is substantially the same as another sequence, but that differs from the other sequence by means of one or more substitutions, additions, and/or deletions, is considered to be an equivalent sequence. Preferably, less than 50%, more preferably less than 25%, and still more preferably less than 10%, of the number of amino acid residues in a sequence are substituted for, added to, or deleted from the protein.

The functional equivalent of an antibody is preferably a chimerized or humanized antibody. A chimerized antibody comprises the variable region of a non-human antibody and the constant region of a human antibody. A humanized antibody comprises the hypervariable region (CDRs) of a non-human antibody. The variable region other than the hypervariable region, e.g., the framework variable region, and the constant region of a humanized antibody are those of a human antibody.

Suitable variable and hypervariable regions of non-human antibodies may be derived from antibodies produced by any non-human mammal in which monoclonal antibodies are made. Suitable examples of mammals other than humans include, for example, rabbits, rats, mice, horses, goats, or primates.

Functional equivalents further include fragments of antibodies that have binding characteristics that are the same as, or are comparable to, those of the whole antibody. Suitable fragments of the antibody include any fragment that comprises a sufficient portion of the hypervariable (i.e., complementarity determining) region to bind specifically, and with sufficient affinity, to EGFR tyrosine kinase to inhibit growth of cells that express such receptors.

Such fragments may, for example, contain one or both Fab fragments or the $F(ab')_2$ fragment. Preferably, the antibody fragments contain all six complementarity determining regions of the whole antibody, although functional fragments containing fewer than all of such regions, such as three, four, or five CDRs, are also included.

In one aspect, the fragments are single chain antibodies, or Fv fragments. Single chain antibodies are polypeptides that comprise at least the variable region of the heavy chain of the antibody linked to the variable region of the light chain, with or without an interconnecting linker. Thus, Fv fragment comprises the entire antibody combining site. These chains may be produced in bacteria or in eukaryotic cells.

The antibodies and functional equivalents may be members of any class of immunoglobulins, such as IgG, IgM, IgA, IgD, or IgE, and the subclasses thereof. In one aspect, the antibodies are members of the IgG1 subclass. The functional equivalents may also be equivalents of combinations of any of the above classes and subclasses.

In one aspect, EGFR antibodies can be selected from chimerized, humanized, fully human, and single chain antibodies derived from the murine antibody 225 described in U.S. Patent No. 4,943,533 to Mendelsohn et al. In one aspect, the 225 derived antibodies have the following hypervariable (CDR) regions of the light and heavy chain, wherein the amino acid sequences are indicated below the nucleotide sequences:

HEAVY CHAIN HYPERVARIABLE REGIONS (VH):

CDR1

AACTATGGTGTACAC (SEQ ID NO: 179)

N Y G V H (SEQ ID NO: 180)

CDR2

GTGATATGGAGTGGTGGAAACACAGACTATAATACACCTTTCACATCC (SEQ ID NO: 181)

V I W S G G N T D Y N T P F T S (SEQ ID NO: 182)

CDR3

GCCCTCACCTACTATGATTACGAGTTTGCTTAC (SEQ ID NO: 183)

A L T Y Y D Y E F A Y (SEQ ID NO: 184)

LIGHT CHAIN HYPERVARIABLE REGIONS (VL):

CDR1

AGGGCCAGTCAGAGTATTGGCACAAACATACAC (SEQ ID NO: 185)

R A S Q S I G T N I H (SEQ ID NO: 186)

CDR2

GCTTCTGAGTCTATCTCT (SEQ ID NO: 187)

A S E S I S (SEQ ID NO: 188)

CDR3

CAACAAAATAATAACTGGCCAACCACG (SEQ ID NO: 189)

Q Q N N N W P T T (SEQ ID NO: 190)

In another aspect, the EGFR antibody can be selected from the antibodies described in U.S. Patent No. 6,235,883 to Jakobovits et al., U.S. Patent No. 5,558,864 to Bendi et al., and U.S. Patent No. 5,891,996 to Mateo de Acosta del Rio et al.

In addition to the biological molecules discussed above, the EGFR modulators useful in the invention may also be small molecules. Any molecule that is not a biological molecule is considered herein to be a small molecule. Some examples of small molecules include organic compounds, organometallic compounds, salts of organic and organometallic compounds, saccharides, amino acids, and nucleotides. Small molecules further include molecules that would otherwise be considered biological molecules, except their molecular weight is not greater than 450. Thus,

small molecules may be lipids, oligosaccharides, oligopeptides, and oligonucleotides and their derivatives, having a molecular weight of 450 or less.

It is emphasized that small molecules can have any molecular weight. They are merely called small molecules because they typically have molecular weights less than 450. Small molecules include compounds that are found in nature as well as synthetic compounds. In one embodiment, the EGFR modulator is a small molecule that inhibits the growth of tumor cells that express EGFR. In another embodiment, the EGFR modulator is a small molecule that inhibits the growth of refractory tumor cells that express EGFR.

Numerous small molecules have been described as being useful to inhibit EGFR. For example, U.S. Patent No. 5,656,655 to Spada et al. discloses styryl substituted heteroaryl compounds that inhibit EGFR. The heteroaryl group is a monocyclic ring with one or two heteroatoms, or a bicyclic ring with 1 to about 4 heteroatoms, the compound being optionally substituted or polysubstituted.

U.S. Patent No. 5,646,153 to Spada et al. discloses bis mono and/or bicyclic aryl heteroaryl, carbocyclic, and heterocarbocyclic compounds that inhibit EGFR.

U.S. Patent No. 5,679,683 to Bridges et al. discloses tricyclic pyrimidine compounds that inhibit the EGFR. The compounds are fused heterocyclic pyrimidine derivatives described at column 3, line 35 to column 5, line 6.

U.S. Patent No. 5,616,582 to Barker discloses quinazoline derivatives that have receptor tyrosine kinase inhibitory activity.

Fry et al., Science 265, 1093-1095 (1994) in Figure 1 discloses a compound having a structure that inhibits EGFR.

Osherov et al. disclose tyrphostins that inhibit EGFR/HER1 and HER 2, particularly those in Tables I, II, III, and IV.

U.S. Patent No. 5,196,446 to Levitzki et al. discloses heteroarylethenediyl or heteroarylethendeiylaryl compounds that inhibit EGFR, particularly from column 2, line 42 to column 3, line 40.

Panek et al., Journal of Pharmacology and Experimental Therapeutics 283, 1433-1444 (1997) discloses a compound identified as PD166285 that inhibits the EGFR, PDGFR, and FGFR families of receptors. PD166285 is identified as 6-(2,6-

dichlorophenyl)-2-(4-(2-diethylaminoethyoxy)phenylamino)-8-methyl-8H-pyrido(2,3-d)pyrimidin-7-one having the structure shown in Figure 1 on page 1436.

BIOMARKERS AND BIOMARKER SETS

The invention includes individual biomarkers and biomarker sets having both diagnostic and prognostic value in disease areas in which signaling through EGFR or the EGFR pathway is of importance, e.g., in cancers or tumors, in immunological disorders, conditions or dysfunction, or in disease states in which cell signaling and/or cellular proliferation controls are abnormal or aberrant. The biomarker sets comprise a plurality of biomarkers such as, for example, a plurality of the biomarkers provided in Table 4 below, that highly correlate with resistance or sensitivity to one or more EGFR modulators.

The biomarker sets of the invention enable one to predict or reasonably foretell the likely effect of one or more EGFR modulators in different biological systems or for cellular responses. The biomarker sets can be used in *in vitro* assays of EGFR modulator response by test cells to predict *in vivo* outcome. In accordance with the invention, the various biomarker sets described herein, or the combination of these biomarker sets with other biomarkers or markers, can be used, for example, to predict how patients with cancer might respond to therapeutic intervention with one or more EGFR modulators.

A biomarker set of cellular gene expression patterns correlating with sensitivity or resistance of cells following exposure of the cells to one or more EGFR modulators provides a useful tool for screening one or tumor samples before treatment with the EGFR modulator. The screening allows a prediction of cells of a tumor sample exposed to one or more EGFR modulators, based on the expression results of the biomarker set, as to whether or not the tumor, and hence a patient harboring the tumor, will or will not respond to treatment with the EGFR modulator.

The biomarker or biomarker set can also be used as described herein for monitoring the progress of disease treatment or therapy in those patients undergoing treatment for a disease involving an EGFR modulator.

The biomarkers serve as targets for the development of therapies for disease treatment. Such targets may be particularly applicable to treatment of breast disease,

such as breast cancers or tumors. Indeed, because these biomarkers are differentially expressed in sensitive and resistant cells, their expression patterns are correlated with relative intrinsic sensitivity of cells to treatment with EGFR modulators. Accordingly, the biomarkers highly expressed in resistant cells may serve as targets for the development of new therapies for the tumors which are resistant to EGFR modulators, particularly EGFR inhibitors.

MICROARRAYS

The invention also includes specialized microarrays, e.g., oligonucleotide microarrays or cDNA microarrays, comprising one or more biomarkers, showing expression profiles that correlate with either sensitivity or resistance to one or more EGFR modulators. Such microarrays can be employed in *in vitro* assays for assessing the expression level of the biomarkers in the test cells from tumor biopsies, and determining whether these test cells are likely to be resistant or sensitive to EGFR modulators. For example, a specialized microarray can be prepared using all the biomarkers, or subsets thereof, as described herein and shown in Table 4. Cells from a tissue or organ biopsy can be isolated and exposed to one or more of the EGFR modulators. Following application of nucleic acids isolated from both untreated and treated cells to one or more of the specialized microarrays, the pattern of gene expression of the tested cells can be determined and compared with that of the biomarker pattern from the control panel of cells used to create the biomarker set on the microarray. Based upon the gene expression pattern results from the cells that underwent testing, it can be determined if the cells show a resistant or a sensitive profile of gene expression. Whether or not the tested cells from a tissue or organ biopsy will respond to one or more of the EGFR modulators and the course of treatment or therapy can then be determined or evaluated based on the information gleaned from the results of the specialized microarray analysis.

ANTIBODIES

The invention also includes antibodies, including polyclonal or monoclonal, directed against one or more of the polypeptide biomarkers. Such antibodies can be used in a variety of ways, for example, to purify, detect, and target the biomarkers of

the invention, including both *in vitro* and *in vivo* diagnostic, detection, screening, and/or therapeutic methods.

KITS

The invention also includes kits for determining or predicting whether a patient would be susceptible or resistant to a treatment that comprises one or more EGFR modulators. The patient may have a cancer or tumor such as, for example, a breast cancer or tumor. Such kits would be useful in a clinical setting for use in testing a patient's biopsied tumor or cancer samples, for example, to determine or predict if the patient's tumor or cancer will be resistant or sensitive to a given treatment or therapy with an EGFR modulator. The kit comprises a suitable container that comprises: one or more microarrays, e.g., oligonucleotide microarrays or cDNA microarrays, that comprise those biomarkers that correlate with resistance and sensitivity to EGFR modulators, particularly EGFR inhibitors; one or more EGFR modulators for use in testing cells from patient tissue specimens or patient samples; and instructions for use. In addition, kits contemplated by the invention can further include, for example, reagents or materials for monitoring the expression of biomarkers of the invention at the level of mRNA or protein, using other techniques and systems practiced in the art such as, for example, RT-PCR assays, which employ primers designed on the basis of one or more of the biomarkers described herein, immunoassays, such as enzyme linked immunosorbent assays (ELISAs), immunoblotting, e.g., Western blots, or *in situ* hybridization, and the like, as further described herein.

APPLICATION OF BIOMARKERS AND BIOMARKER SETS

The biomarkers and biomarker sets may be used in different applications. Biomarker sets can be built from any combination of biomarkers listed in Table 4 to make predictions about the likely effect of any EGFR modulator in different biological systems. The various biomarkers and biomarker sets described herein can be used, for example, as diagnostic or prognostic indicators in disease management, to predict how patients with cancer might respond to therapeutic intervention with compounds that modulate the EGFR, and to predict how patients might respond to

therapeutic intervention that modulates signaling through the entire EGFR regulatory pathway.

While the data described herein were generated in cell lines that are routinely used to screen and identify compounds that have potential utility for cancer therapy, the biomarkers have both diagnostic and prognostic value in other diseases areas in which signaling through EGFR or the EGFR pathway is of importance, e.g., in immunology, or in cancers or tumors in which cell signaling and/or proliferation controls have gone awry.

In the examples described below, the sensitivity and resistance classifications in the twenty two colon cell lines were similar for the two EGFR modulators tested. Therefore, the biomarkers of the invention are expected to have both diagnostic and prognostic value for other compounds that modulate EGFR or the EGFR signaling pathways.

Those having skill in the pertinent art will appreciate that the EGFR signaling pathway is used and functional in cell types other than cell lines of colon tissue. Therefore, the described biomarkers are expected to have utility for predicting drug sensitivity or resistance to compounds that interact with or inhibit the EGFR activity in cells from other tissues or organs associated with a disease state, or cancers or tumors derived from other tissue types. Non-limiting examples of such cells, tissues and organs include breast, colon, lung, prostate, testes, ovaries, cervix, esophagus, pancreas, spleen, liver, kidney, stomach, lymphocytic and brain, thereby providing a broad and advantageous applicability to the biomarkers described herein. Cells for analysis can be obtained by conventional procedures as known in the art, for example, tissue biopsy, aspiration, sloughed cells, e.g., colonocytes, clinical or medical tissue or cell sampling procedures.

In accordance with the invention, cells from a patient tissue sample, e.g., a tumor or cancer biopsy, can be assayed to determine the expression pattern of one or more biomarkers prior to treatment with one or more EGFR modulators. Success or failure of a treatment can be determined based on the biomarker expression pattern of the cells from the test tissue (test cells), e.g., tumor or cancer biopsy, as being relatively similar or different from the expression pattern of a control set of the one or more biomarkers. Thus, if the test cells show a biomarker expression profile which

corresponds to that of the biomarkers in the control panel of cells which are sensitive to the EGFR modulator, it is highly likely or predicted that the individual's cancer or tumor will respond favorably to treatment with the EGFR modulator. By contrast, if the test cells show a biomarker expression pattern corresponding to that of the biomarkers of the control panel of cells which are resistant to the EGFR modulator, it is highly likely or predicted that the individual's cancer or tumor will not respond to treatment with the EGFR modulator.

The invention also provides a method of monitoring the treatment of a patient having a disease treatable by one or more EGFR modulators. The isolated test cells from the patient's tissue sample, e.g., a tumor biopsy or tumor sample, can be assayed to determine the expression pattern of one or more biomarkers before and after exposure to an EGFR modulator wherein, preferably, the EGFR modulator is an EGFR inhibitor. The resulting biomarker expression profile of the test cells before and after treatment is compared with that of one or more biomarkers as described and shown herein to be highly expressed in the control panel of cells that are either resistant or sensitive to an EGFR modulator. Thus, if a patient's response is sensitive to treatment by an EGFR modulator, based on correlation of the expression profile of the one or biomarkers, the patient's treatment prognosis can be qualified as favorable and treatment can continue. Also, if, after treatment with an EGFR modulator, the test cells don't show a change in the biomarker expression profile corresponding to the control panel of cells that are sensitive to the EGFR modulator, it can serve as an indicator that the current treatment should be modified, changed, or even discontinued. This monitoring process can indicate success or failure of a patient's treatment with an EGFR modulator and such monitoring processes can be repeated as necessary or desired.

The biomarkers of the invention can be used to predict an outcome prior to having any knowledge about a biological system. Essentially, a biomarker can be considered to be a statistical tool. Biomarkers are useful primarily in predicting the phenotype that is used to classify the biological system. In an embodiment of the invention, the goal of the prediction is to classify cancer cells as having an active or inactive EGFR pathway. Cancer cells with an inactive EGFR pathway can be considered resistant to treatment with an EGFR modulator. An inactive EGFR

pathway is defined herein as a non-significant expression of the EGFR or by a classification as "resistant" or "sensitive" based on the IC_{50} value of each colon cell line to a compound (EGFR inhibitor compound BMS-461453) exemplified herein.

A number of the biomarker described herein are known to be regulated by EGFR, e.g., mucin 2 (J Biol Chem. 2002 Aug 30;277(35):32258-67). Another biomarker, betacellulin, is know to be an EGFR ligand (Biochem Biophys Res Commun. 2002 Jun 28;294(5):1040-6). A functional relationship of the top biomarkers to the EGFR is expected, since biomarkers that contribute to high biomarker accuracy are likely to play a functional role in the pathway that is being modulated. For example, Perception therapy (i.e., antibody that binds to the Her2 receptor and prevents function via internalization) is indicated when the Her2 gene is overexpressed. It is unlikely that a therapy will have any therapeutic effect if the target enzyme is not expressed.

However, although the complete function of all of the biomarkers are not currently known, some of the biomarkers are likely to be directly or indirectly involved in the EGFR signaling pathway. In addition, some of the biomarkers may function in the metabolic or other resistance pathways specific to the EGFR modulators tested. Notwithstanding, knowledge about the function of the biomarkers is not a requisite for determining the accuracy of a biomarker according to the practice of the invention.

DISCOVERY OF BIOMARKERS

An approach has been discovered in which biomarkers were identified whose expression patterns, in a subset of cell lines, correlated to and can be used as an *in vitro* marker of cellular response to treatment or therapy with one compound, or with a combination or series of compounds, that are known to inhibit or activate the function of a protein, enzyme, or molecule (e.g., a receptor) that is directly or indirectly involved in cell proliferation, cell responses to external stimuli, (such as ligand binding), or signal transduction, e.g., a receptor tyrosine kinase. Preferred are antagonists or inhibitors of the function of a given protein, e.g., a receptor tyrosine kinase.

Two analytical strategies were deployed to discover biomarkers useful for predicting the sensitivity or resistance of cancer cells to treatment with one or more EGFR modulators. FIG. 1 illustrates the EGFR biomarker identification and prioritization strategy. In one strategy, the mRNA expression level of EGFR was used to identify six colon cancer cell lines with, inferred from the mRNA expression level, no significant presence of the EGFR protein and hence no significant activity of the EGFR pathway (FIG. 2A). In subsequent analyses, biomarkers were identified that had no significant mRNA expression level in the six cell lines and no inferred presence of the EGFR protein. Further, it was required that these biomarkers would have a significant mRNA expression level in at least six other cell lines.

In a second strategy, an EGFR specific tyrosine kinase inhibitor compound was used to determine compound sensitivity in a panel of twenty two colon cancer cell lines following exposure of the cells to the compound. Some of the cell lines were determined to be resistant to treatment with the inhibitor compound, while others were determined to be sensitive to the inhibitor (FIG. 2B). A subset of the cell lines examined provided an expression pattern or profile of biomarkers that correlated to a response by the cells to the EGFR inhibitor compound as well as the absence of significant EGFR expression as thus could serve as biomarkers.

By combining the use of EGFR co-regulation studies in tumor cells with experimental studies in cultured cells as a model of *in vivo* effects, the invention advantageously focuses on cell-intrinsic properties that are exposed in cell culture to identify biomarkers that predict compound sensitivity and resistance. The discovery and identification of biomarkers in tumor cells and cell lines assayed *in vitro* can be used to predict responses to one or more EGFR modulators *in vivo* and, thus, can be extended to clinical situations in which the same biomarkers are used to predict patients' responses to one or more EGFR modulators and treatments comprising one or more EGFR modulators.

As described in the examples below, oligonucleotide microarrays were used to measure the expression levels of over 44,792 probe sets in a panel of thirty one untreated colon cancer cell lines for which the expression status of the EGFR and the drug sensitivity to EGFR inhibitor compounds was determined. This analysis was performed to determine whether the gene expression signatures of untreated cells

were sufficient for the prediction of sensitivity of the disease to inhibition of the EGFR by small molecule or biological molecule compounds. Through data analysis, biomarkers were identified whose expression levels were found to be highly counter-correlated with the status of the EGFR and correlated with the drug sensitivity. In addition, the treatment of cells with a small molecule EGFR inhibitor also provided gene expression signatures predictive of sensitivity to the compound.

The means of performing the gene expression and biomarker identification analyses embraced by the invention is described in further detail and without limitation below.

IC_{50} Determination and Phenotype Classification Based on Sensitivity of Twenty-two Colon Cancer Cell lines to EGFR Inhibitor Compounds

Twenty two colon cell lines were treated with a small molecule EGFR inhibitor (BMS-461453) to determine the individual IC_{50} value. The IC_{50} for each cell line was assessed by MTS assays. The average IC_{50} values along with standard deviations were calculated from two to five individual determinations for each cell line. As shown in FIG. 2B, a 4-fold variation in the IC_{50} values was observed for the small molecule EGFR inhibitor among the 22 colon cancer cell lines. The IC_{50} unit is μM.

All cell lines with at least a 1.75 fold lower IC_{50} than the most resistant cell lines were considered to be sensitive to treatment with the small molecule EGFR inhibitor. FIG. 2B represents the resistance/sensitivity classifications of the twenty-two colon cell lines to the small molecule EGFR inhibitor. Five cell lines were classified as sensitive and seventeen cell lines as resistant.

Description of the Strategy for Identifying Biomarkers

Biomarkers were discovered based on two criteria: (i) the correlation of their mRNA expression level to the expression of EGFR in cell lines with insignificant EGFR expression and (ii) the correlation of the IC_{50} values for the small molecule EGFR inhibitor BMS-461453 with gene expression levels.

For each of these two biomarker selection strategies, two independent "discovery" probe set lists were established by using statistical filters with different

stringency levels to identify genes whose expression correlated with either EGFR status or IC_{50} value. These statistical methods are described below and resulted in four discovery probe set lists: EGFR-A and EGFR-B (correlation with no significant EGFR expression) and IC-50-A, IC-50-B (correlation with IC_{50} expression), the A-lists containing probe sets selected by more stringent conditions. To then establish two biomarker probe set lists, probe sets that appeared in both EGFR-A and IC-50 B were selected (Biomarker Probe Set List A, Table 2) and probe sets that appeared in both EGFR-B and IC-50-A were selected (Biomarker Probe Set List B, Table 3).

Identifying Genes that Significantly Correlate with EGFR status classification

RT-PCR expression data for EGFR were obtained from thirty one colon cancer cell lines and six cell lines with a significantly lower expression level of EGFR compared to the other cell lines were identified as described in Example 1 below. (FIG. 2A). Expression profiling data of 44,792 probe sets represented on the HG-U133 array set for all thirty one untreated colon cancer cell lines were obtained and analyzed for the identification of probe sets which would be correlated with the above described six cell lines with no significant mRNA expression of EGFR. For the discovery probe set list EGFR-A, all probe sets which were judged to be absent by the Affymetrix Mas 5.0 software in six of the six colon cancer cell lines with significantly lower expression of EGFR were identified. Second, it was required that these probe sets would be judged to be present in at least six cell lines of the twenty five cell lines classified as having significant mRNA expression of the EGFR. This analytical strategy resulted in the identification of 280 probe sets that could be analyzed in comparison to the discovery probe set list IC-50-B.

The discovery probe set list EGFR-B was generated by selecting all probe sets which were judged to be absent by the Affymetrix Mas 5.0 software in five of the six colon cancer cell lines with significantly lower expression of EGFR and which would be present in at least six cell lines of the twenty five cell lines classified as having significant mRNA expression of the EGFR. Discovery probe set list EGR-B contains 1,852 probe sets (U133A: 876; U133B: 976).

Identifying Genes that Significantly Correlate with Drug Resistance/Sensitivity Classification

Expression profiling data of 44,792 probe sets represented on the HG-U133 array set for twenty two untreated colon cell lines were obtained and preprocessed as described in Example 1 below. These data were analyzed using the Student's TTEST to identify genes whose expression patterns were strongly correlated with the drug resistance/sensitivity classification. Table 1 provides the resistance/sensitivity phenotype classification of the twenty two colon cell lines for the EGFR antagonist BMS-461453 based on the IC_{50} results. The mean IC_{50} values along with standard deviations (SD) were calculated from 2 to 5 individual determinations for each cell line as shown. The mean IC_{50} across the twenty two colon cell lines for BMS-461453 was calculated and used to normalize the IC_{50} data for each cell line. All cell lines with at least a 1.75 fold lower IC_{50} than the most resistant cell lines were considered to be sensitive to treatment with BMS-461453. The cell lines designated with an asterisk are defined as being sensitive to the drug treatment.

TABLE 1 - Resistance/Sensitivity Phenotype Classification of Twenty Two Colon Cell Lines

Cell lines	IC_{50} (μM)	SD
CCD_33C0*	2	1.28
LOVO*	2.3	2.28
*LS174T**	3.5	1.93
Caco2*	5.5	3.97
SW403*	5.7	4.94
CCD18Co	7.1	3.84
SW837	7.2	3.30
Sk-Co-1	9	2.02
MIP	9.7	0.52
SW1417	10	0.00
HT-29	10	0.00
T84	10	0.00
CX-1	10	0.00
Colo-205	10	0.00
Colo-201	10	0.00
Colo320HSR	10	0.00
HCT8	10	0.00
Colo320DM	10	0.00
SW480	10	0.00
HCT116	10	0.00
SW620	10	0.00
HCT116S542	10	0.00

An "idealized expression pattern" corresponds to a gene that is uniformly high in one class (e.g., sensitive) and uniformly low in the other (e.g., resistant). Initially, a Student TTEST was performed in which a T value was obtained for each probe set. Once a T value was generated, its corresponding confidence value (P) was found on a standard table of significance. The confidence value is a measure of the probability to observe a certain mean expression difference between two groups by chance alone and is obtained using the following formula:

$$T(g.c) = (X_1 - X_2) / (var_1/n_1 + var_2/n_2)^{1/2}$$

wherein,

T(g,c) represents the T value between expression for gene g and the sensitivity/resistance classification c;

X_1 represents mean gene expression level of samples in class 1;

X_2 represents mean gene expression level of samples in class 2;

var_1 represents variance of gene expression for samples in class 1;

var_2 represents variance of gene expression for samples in class 2;

n_1 represents number of samples in class 1;

n_2 represents number of samples in class 2; and

corresponding confidence value (P) for T values are obtained from a standard table of significance.

To generate discovery probe set list IC-50-B, a confidence value of 0.05 or lower was used as the cut off for probe sets to be included in the list. Discovery probe set list IC-50-B contains 5,050 probe sets (U133A: 2,498; U133B: 2,552).

Discovery probe set list IC-50-A was generated using the Pearson correlation coefficient (a dimensionless index that ranges from -1.0 to 1.0). This value was calculated by treating the IC_{50} data as continuous variables and by utilizing a linear regression model to correlate gene expression levels with IC_{50} values for twenty-two colon cell lines. Probe sets with a correlation coefficient less than –0.5 were selected ($p < 0.02$), a total of 902 probe sets (U133A: 467; U133B: 435).

Finally, two separate biomarker probe set lists were generated, biomarker probe set lists A and B, by identifying probe sets which were present in EGFR-A and IC-50-B (Biomarker Probe Set List A) (Table 2) or were present in EGFR-B and IC-50-A (Biomarker Probe Set List B) (Table 3).

The biomarker probe set list A (Table 2) contains a total of 74 probe sets (U133A: 43; U133B: 31) and provides the polynucleotides identified to be biomarkers of EGFR antagonist sensitivity employing strategy A. With strategy A, polynucleotides were required to satisfy a stringent criteria for EGFR status coregulation and a less stringent condition for correlation to IC_{50} values. Namely, the polynucleotides had to be called absent by the Affymetrix software in six out of the

six cell lines with lowest expression of EGFR and be differentially expressed in the sensitive and resistance cell lines with a P value equal to or less than 0.05.

TABLE 2 - Biomarker Probe Set List A

Unigene Title	Affymetrix Description	Affymetrix probe set
hemoglobin, alpha 1	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:NM_001935.1	203716_s_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)	gb:NM_005518.1 /DEF=Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2(mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:NM_005518.1	204607_at
mucin 2, intestinal/tracheal	gb:NM_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:NM_002457.1 gb:L21998.1	204673_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	gb:NM_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane conductanceregulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995	205043_at

	/UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:NM_000492.2	
CUG triplet repeat, RNA-binding protein 2	Consensus includes gb:N36839 /FEA=EST /DB_XREF=gi:1157981 /DB_XREF=est:yy35f07.s1 /CLONE=IMAGE:273253 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202156_s_at
nuclear receptor subfamily 3, group C, member 2	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215702_s_at
cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2	gb:NM_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily IIJ (arachidonic acidepoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:NM_000775.1	205073_at
cystatin S	gb:NM_001899.1 /DEF=Homo sapiens cystatin S (CST4), mRNA. /FEA=mRNA /GEN=CST4 /PROD=cystatin S /DB_XREF=gi:4503108 /UG=Hs.56319 cystatin S /FL=gb:NM_001899.1	206994_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213993_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase,	gb:NM_022969.1 /DEF=Homo sapiens fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome,	203638_s_at

keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2), transcript variant 2, mRNA. /FEA=mRNA /GEN=FGFR2 /PROD=fibroblast growth factor receptor 2, isoform 2precursor /DB_XREF=gi:13186252 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022969.1 gb:M97193.1 gb:M80634.1	
mucin 3B	Consensus includes gb:AB038783.1 /DEF=Homo sapiens MUC3B mRNA for intestinal mucin, partial cds. /FEA=mRNA /GEN=MUC3B /PROD=intestinal mucin /DB_XREF=gi:9929917 /UG=Hs.129782 mucin 3A, intestinal	214898_x_at
AA	Consensus includes gb:AV728958 /FEA=EST /DB_XREF=gi:10838379 /DB_XREF=est:AV728958 /CLONE=HTCBYF04 /UG=Hs.150443 KIAA0320 protein	212703_at
CUG triplet repeat, RNA-binding protein 2	gb:NM_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202158_s_at
spondin 1, (f-spondin) extracellular matrix protein	gb:AB051390.1 /DEF=Homo sapiens mRNA for VSGPF-spondin, complete cds. /FEA=mRNA /PROD=VSGPF-spondin /DB_XREF=gi:11320819 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein /FL=gb:AB051390.1	209437_s_at
mucin 3B	Consensus includes gb:AF113616 /DEF=Homo sapiens intestinal mucin 3 (MUC3) gene, partial cds /FEA=mRNA /DB_XREF=gi:6466800 /UG=Hs.129782 mucin 3A, intestinal	214676_x_at
EphA1	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
matrilin 3	gb:NM_002381.2 /DEF=Homo sapiens matrilin 3 (MATN3) precursor, mRNA. /FEA=mRNA /GEN=MATN3 /PROD=matrilin 3 precursor /DB_XREF=gi:13518040 /UG=Hs.278461	206091_at

	matrilin 3 /FL=gb:NM_002381.2	
bone morphogenetic protein 2	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
interferon consensus sequence binding protein 1	Consensus includes gb:AI073984 /FEA=EST /DB_XREF=gi:3400628 /DB_XREF=est:oy66c05.x1 /CLONE=IMAGE:1670792 /UG=Hs.14453 interferon consensus sequence binding protein 1 /FL=gb:M91196.1 gb:NM_002163.1	204057_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1 /CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	221872_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215703_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	gb:M87771.1 /DEF=Human secreted fibroblast growth factor receptor (K-sam-III) mRNA, complete cds. /FEA=mRNA /GEN=K-sam-III /PROD=fibroblast growth factor receptor /DB_XREF=gi:186781 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022970.1 gb:M87771.1	208228_s_at
myosin, heavy polypeptide 13, skeletal muscle	gb:NM_003802.1 /DEF=Homo sapiens myosin, heavy polypeptide 13, skeletal muscle (MYH13), mRNA. /FEA=mRNA /GEN=MYH13 /PROD=myosin, heavy polypeptide 13, skeletal muscle /DB_XREF=gi:11321578 /UG=Hs.278488 myosin, heavy polypeptide 13, skeletal muscle /FL=gb:NM_003802.1	208208_at

	gb:AF111782.2	
ESTs, Weakly similar to I38022 hypothetical protein [H.sapiens]	Consensus includes gb:AW675655 /FEA=EST /DB_XREF=gi:7540890 /DB_XREF=est:ba52e01.x1 /CLONE=IMAGE:2900184 /UG=Hs.314158 ESTs	222354_at
hypothetical protein FLJ20174	gb:NM_017699.1 /DEF=Homo sapiens hypothetical protein FLJ20174 (FLJ20174), mRNA. /FEA=mRNA /GEN=FLJ20174 /PROD=hypothetical protein FLJ20174 /DB_XREF=gi:8923170 /UG=Hs.114556 hypothetical protein FLJ20174 /FL=gb:NM_017699.1	219734_at
PTPRF interacting protein, binding protein 2 (liprin beta 2)	Consensus includes gb:AI692180 /FEA=EST /DB_XREF=gi:4969520 /DB_XREF=est:wd37f06.x1 /CLONE=IMAGE:2330339 /UG=Hs.12953 PTPRF interacting protein, binding protein 2 (liprin beta 2)	212841_s_at
ribonuclease, RNase A family, 1 (pancreatic)	gb:NM_002933.1 /DEF=Homo sapiens ribonuclease, RNase A family, 1 (pancreatic) (RNASE1), mRNA. /FEA=mRNA /GEN=RNASE1 /PROD=ribonuclease, RNase A family, 1 (pancreatic) /DB_XREF=gi:4506546 /UG=Hs.78224 ribonuclease, RNase A family, 1 (pancreatic) /FL=gb:BC005324.1 gb:NM_002933.1 gb:D26129.1	201785_at
hairless (mouse) homolog	gb:NM_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:NM_018411.1	220163_s_at
nuclear receptor subfamily 5, group A, member 2	Consensus includes gb:AF228413.1 /DEF=Homo sapiens hepatocyte transcription factor mRNA, 3UTR. /FEA=mRNA /DB_XREF=gi:7677372 /UG=Hs.183123 nuclear receptor subfamily 5, group A, member 2 /FL=gb:U93553.1 gb:AB019246.1 gb:AF124247.1	210174_at
superoxide dismutase 3, extracellular	gb:NM_003102.1 /DEF=Homo sapiens superoxide dismutase 3, extracellular (SOD3), mRNA. /FEA=mRNA /GEN=SOD3 /PROD=superoxide dismutase 3, extracellular	205236_x_at

	/DB_XREF=gi:4507150 /UG=Hs.2420 superoxide dismutase 3, extracellular /FL=gb:J02947.1 gb:NM_003102.1	
zinc finger protein 137 (clone pHZ-30)	gb:NM_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ-30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:NM_003438.1 gb:U09414.1	207394_at
Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	Consensus includes gb:AL049983.1 /DEF=Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042). /FEA=mRNA /DB_XREF=gi:4884234 /UG=Hs.240136 Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	217288_at
Hermansky-Pudlak syndrome	Consensus includes gb:AL022313 /DEF=Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene f... /FEA=CDS_3 /DB_XREF=gi:4200326 /UG=Hs.272270 Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene for a nov	217354_s_at
peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase	gb:NM_018441.1 /DEF=Homo sapiens peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase (HSA250303), mRNA. /FEA=mRNA /GEN=HSA250303 /PROD=peroxisomal trans 2-enoyl CoA reductase;putative short chain alcohol dehydrogenase /DB_XREF=gi:8923751 /UG=Hs.281680 peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase /FL=gb:NM_018441.1	221142_s_at
BTG family, member 2	gb:NM_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:NM_006763.1	201236_s_at
phosducin	gb:M33478.1 /DEF=Human 33-kDa phototransducing protein mRNA, complete cds.	211496_s_at

	/FEA=mRNA /DB_XREF=gi:177186 /UG=Hs.550 phosducin /FL=gb:NM_022577.1 gb:M33478.1 gb:AF076465.1	
Rho GTPase activating protein 8	gb:NM_015366.1 /DEF=Homo sapiens Rho GTPase activating protein 8 (ARHGAP8), mRNA. /FEA=mRNA /GEN=ARHGAP8 /PROD=Rho GTPase activating protein 8 /DB_XREF=gi:7656903 /UG=Hs.102336 Rho GTPase activating protein 8 /FL=gb:NM_015366.1	205980_s_at
Homo sapiens clone 24707 mRNA sequence	Consensus includes gb:AW593996 /FEA=EST /DB_XREF=gi:7281254 /DB_XREF=est:hg41g06.x1 /CLONE=IMAGE:2948218 /UG=Hs.124969 Homo sapiens clone 24707 mRNA sequence	213256_at
caspase 10, apoptosis-related cysteine protease	gb:NM_001230.1 /DEF=Homo sapiens caspase 10, apoptosis-related cysteine protease (CASP10), mRNA. /FEA=mRNA /GEN=CASP10 /PROD=caspase 10, apoptosis-related cysteine protease /DB_XREF=gi:4502568 /UG=Hs.5353 caspase 10, apoptosis-related cysteine protease /FL=gb:U60519.1 gb:NM_001230.1	205467_at
KIAA0690 protein	Consensus includes gb:AK000238.1 /DEF=Homo sapiens cDNA FLJ20231 fis, clone COLF5511, highly similar to AB014590 Homo sapiens mRNA for KIAA0690 protein. /FEA=mRNA /DB_XREF=gi:7020188 /UG=Hs.60103 KIAA0690 protein	216360_x_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:3852062, mRNA, complete cds	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
ESTs	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at
ESTs	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at

hypothetical protein FLJ23045	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at
regenerating gene type IV	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
ESTs	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
hypothetical protein MGC20702	Consensus includes gb:AK002203.1 /DEF=Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786. /FEA=mRNA /DB_XREF=gi:7023932 /UG=Hs.10260 Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786	226992_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY [H.sapiens]	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
ESTs	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376	231148_at

	ESTs	
anterior gradient 2 (Xenepus laevis) homolog	Consensus includes gb:AI922323 /FEA=EST /DB_XREF=gi:5658287 /DB_XREF=est:wn90h03.x1 /CLONE=IMAGE:2453141 /UG=Hs.293380 ESTs	228969_at
ESTs	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
hypothetical protein FLJ22233	Consensus includes gb:AI339568 /FEA=EST /DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	222727_s_at
GalNAc alpha-2, 6-sialyltransferase I, long form	Consensus includes gb:Y11339.2 /DEF=Homo sapiens mRNA for GalNAc alpha-2, 6-sialyltransferase I, long form. /FEA=mRNA /PROD=GalNAc alpha-2,6-sialyltransferase I /DB_XREF=gi:7576275 /UG=Hs.105352 GalNAc alpha-2, 6-sialyltransferase I, long form	227725_at
ESTs	Consensus includes gb:AI917390 /FEA=EST /DB_XREF=gi:5637245 /DB_XREF=est:ts79a05.x1 /CLONE=IMAGE:2237456 /UG=Hs.99415 ESTs	240964_at
Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	Consensus includes gb:AK026404.1 /DEF=Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA. /FEA=mRNA /DB_XREF=gi:10439257 /UG=Hs.271819 Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	232321_at
Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	Consensus includes gb:AK026984.1 /DEF=Homo sapiens cDNA: FLJ23331 fis, clone HEP12664. /FEA=mRNA /DB_XREF=gi:10439980 /UG=Hs.50742 Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	229021_at
ESTs	Consensus includes gb:AA827649 /FEA=EST /DB_XREF=gi:2900090 /DB_XREF=est:od01a12.s1 /CLONE=IMAGE:1357918 /UG=Hs.105317 ESTs	235515_at
prostate cancer	Consensus includes gb:AA633076 /FEA=EST	226167_at

associated protein 7	/DB_XREF=gi:2556490 /DB_XREF=est:nq38a06.s1 /CLONE=IMAGE:1146130 /UG=Hs.27495 prostate cancer associated protein 7	
ESTs	Consensus includes gb:N37023 /FEA=EST /DB_XREF=gi:1158165 /DB_XREF=est:yy40d03.s1 /CLONE=IMAGE:273701 /UG=Hs.235883 ESTs	225407_at
ESTs, Weakly similar to I38588 reverse transcriptase homolog [H.sapiens]	Consensus includes gb:AI864053 /FEA=EST /DB_XREF=gi:5528160 /DB_XREF=est:wj55h10.x1 /CLONE=IMAGE:2406787 /UG=Hs.39972 ESTs, Weakly similar to I38588 reverse transcriptase homolog H.sapiens	235678_at
ESTs, Weakly similar to JX0331 laurate omega-hydroxylase [H.sapiens]	Consensus includes gb:AA557324 /FEA=EST /DB_XREF=gi:2327801 /DB_XREF=est:nl81a02.s1 /CLONE=IMAGE:1057034 /UG=Hs.26040 ESTs, Weakly similar to fatty acid omega-hydroxylase H.sapiens	227702_at
ESTs	Consensus includes gb:BF594323 /FEA=EST /DB_XREF=gi:11686647 /DB_XREF=est:7h79g07.x1 /CLONE=IMAGE:3322236 /UG=Hs.158989 ESTs	238103_at
ESTs, Weakly similar to JE0350 Anterior gradient-2 [H.sapiens]	Consensus includes gb:AI827789 /FEA=EST /DB_XREF=gi:5448449 /DB_XREF=est:wf33a07.x1 /CLONE=IMAGE:2357364 /UG=Hs.100686 ESTs, Weakly similar to JE0350 Anterior gradient-2 H.sapiens	228241_at
ESTs	Consensus includes gb:AI968097 /FEA=EST /DB_XREF=gi:5764915 /DB_XREF=est:wu13a12.x1 /CLONE=IMAGE:2516830 /UG=Hs.131360 ESTs	237835_at
ESTs	Consensus includes gb:H05025 /FEA=EST /DB_XREF=gi:868577 /DB_XREF=est:yl74g12.s1 /CLONE=IMAGE:43864 /UG=Hs.323767 ESTs	241874_at
Homo sapiens, Similar to RIKEN cDNA 1110060O18 gene, clone MGC:17236 IMAGE:386413	Consensus includes gb:AA524690 /FEA=EST /DB_XREF=gi:2265618 /DB_XREF=est:ng38e07.s1 /CLONE=IMAGE:937092 /UG=Hs.294143 ESTs, Weakly similar to predicted using Genefinder C.elegans	226168_at

7, mRNA, complete cds		
ESTs	Consensus includes gb:AI300126 /FEA=EST /DB_XREF=gi:3959472 /DB_XREF=est:qn54f02.x1 /CLONE=IMAGE:1902075 /UG=Hs.257858 ESTs	240830_at
Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	Consensus includes gb:AA129774 /FEA=EST /DB_XREF=gi:1690185 /DB_XREF=est:zl16h09.s1 /CLONE=IMAGE:502145 /UG=Hs.288905 Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	227019_at
ESTs	Consensus includes gb:AW024656 /FEA=EST /DB_XREF=gi:5878186 /DB_XREF=est:wu78h05.x1 /CLONE=IMAGE:2526201 /UG=Hs.233382 ESTs, Moderately similar to AF119917 62 PRO2822 H.sapiens	242358_at

The biomarker probe set list B (Table 3) contains 95 probe sets (U133A: 47; U133B 48). The biomarker probe set list B contains polynucleotides identified to be biomarkers of EGFR antagonist sensitivity employing strategy B. In strategy B, polynucleotides were required to satisfy a stringent criteria for correlation to IC_{50} values and a less stringent condition for EGFR status coregulation. Namely, the polynucleotides had to have a Pearsons correlation of -0.5 or less with respect to IC_{50} and be called absent by the Affymetrix software in 5 out of the 6 cell lines with lowest expression of EGFR.

TABLE 3 - Biomarker Probe Set List B

Unigene Title	Affymetrix Description	Affymetrix probe set
dopa decarboxylase (aromatic L-amino acid decarboxylase)	Consensus includes gb:AW772056 /FEA=EST /DB_XREF=gi:7704118 /DB_XREF=est:hn64g06.x1 /CLONE=IMAGE:3032698 /UG=Hs.150403 dopa decarboxylase (aromatic L-amino acid decarboxylase)	214347_s_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette	gb:NM_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane	205043_at

(sub-family C, member 7)	conductanceregulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:NM_000492.2	
carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen)	gb:BC005008.1 /DEF=Homo sapiens, carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen), clone MGC:10467, mRNA, complete cds. /FEA=mRNA /PROD=carcinoembryonic antigen-related cell adhesionmolecule 6 (non-specific cross reacting antigen) /DB_XREF=gi:13477106 /UG=Hs.73848 carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) /FL=gb:BC005008.1 gb:M18216.1 gb:M29541.1 gb:NM_002483.1	203757_s_at
hypothetical protein FLJ20075	gb:NM_017655.1 /DEF=Homo sapiens hypothetical protein FLJ20075 (FLJ20075), mRNA. /FEA=mRNA /GEN=FLJ20075 /PROD=hypothetical protein FLJ20075 /DB_XREF=gi:8923083 /UG=Hs.205058 hypothetical protein FLJ20075 /FL=gb:NM_017655.1	219970_at
ATPase, Class V, type 10B	Consensus includes gb:AW006935 /FEA=EST /DB_XREF=gi:5855713 /DB_XREF=est:wt08b11.x1 /CLONE=IMAGE:2506845 /UG=Hs.109358 ATPase, Class V, type 10B	214070_s_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215702_s_at
HERV-H LTR-associating 2	gb:NM_007072.1 /DEF=Homo sapiens HERV-H LTR-associating 2 (HHLA2), mRNA. /FEA=mRNA /GEN=HHLA2 /PROD=HERV-H LTR-associating 2 /DB_XREF=gi:5901963 /UG=Hs.252351 HERV-H LTR-associating 2 /FL=gb:AF126162.1 gb:NM_007072.1	220812_s_at
AA	Consensus includes gb:AV728958 /FEA=EST /DB_XREF=gi:10838379 /DB_XREF=est:AV728958 /CLONE=HTCBYF04 /UG=Hs.150443 KIAA0320 protein	212703_at

hemoglobin, alpha 2	Consensus includes gb:T50399 /FEA=EST /DB_XREF=gi:652259 /DB_XREF=est:yb30b11.s1 /CLONE=IMAGE:72669 /UG=Hs.251577 hemoglobin, alpha 1	214414_x_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213993_at
hemoglobin, alpha 1	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5	gb:NM_002639.1 /DEF=Homo sapiens serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5), mRNA. /FEA=mRNA /GEN=SERPINB5 /PROD=serine (or cysteine) proteinase inhibitor, cladeB (ovalbumin), member 5 /DB_XREF=gi:4505788 /UG=Hs.55279 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 /FL=gb:NM_002639.1 gb:U04313.1	204855_at
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)	gb:NM_005518.1 /DEF=Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2(mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:NM_005518.1	204607_at
anterior gradient 2 (Xenepus laevis) homolog	gb:AF088867.1 /DEF=Homo sapiens putative secreted protein XAG mRNA, complete cds. /FEA=mRNA /PROD=putative secreted protein XAG /DB_XREF=gi:6652811 /UG=Hs.91011 anterior gradient 2 (Xenepus laevis) homolog /FL=gb:AF007791.1 gb:AF038451.1 gb:NM_006408.1 gb:AF088867.1	209173_at
FXYD domain-containing ion transport regulator 3	gb:BC005238.1 /DEF=Homo sapiens, FXYD domain-containing ion transport regulator 3, clone MGC:12265, mRNA, complete cds. /FEA=mRNA /PROD=FXYD domain-containing ion transport regulator3 /DB_XREF=gi:13528881 /UG=Hs.301350 FXYD domain-containing ion transport regulator	202489_s_at

	3 /FL=gb:NM_005971.2 gb:BC005238.1	
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:NM_001935.1	203716_s_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	Consensus includes gb:W60595 /FEA=EST /DB_XREF=gi:1367354 /DB_XREF=est:zc91b04.s1 /CLONE=IMAGE:338479 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)	215703_at
EphA1	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
spondin 1, (f-spondin) extracellular matrix protein	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
CUG triplet repeat, RNA-binding protein 2	gb:NM_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202158_s_at
DKFZP434C091 protein	Consensus includes gb:AL080170.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C091 (from clone DKFZp434C091); partial cds. /FEA=mRNA /GEN=DKFZp434C091 /PROD=hypothetical protein /DB_XREF=gi:5262639 /UG=Hs.51692 DKFZP434C091 protein	215047_at
mucin 3B	Consensus includes gb:AF113616 /DEF=Homo sapiens intestinal mucin 3 (MUC3) gene, partial cds /FEA=mRNA /DB_XREF=gi:6466800 /UG=Hs.129782 mucin 3A, intestinal	214676_x_at
potassium channel,	gb:U90065.1 /DEF=Human potassium channel KCNO1 mRNA, complete cds. /FEA=mRNA	204678_s_at

subfamily K, member 1 (TWIK-1)	/PROD=potassium channel KCNO1 /DB_XREF=gi:1916294 /UG=Hs.79351 potassium channel, subfamily K, member 1 (TWIK-1) /FL=gb:U33632.1 gb:U90065.1 gb:U76996.1 gb:NM_002245.1	
nuclear receptor subfamily 3, group C, member 2	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
BTG family, member 2	gb:NM_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:NM_006763.1	201236_s_at
G protein-coupled receptor 49	gb:AF062006.1 /DEF=Homo sapiens orphan G protein-coupled receptor HG38 mRNA, complete cds. /FEA=mRNA /PROD=orphan G protein-coupled receptor HG38 /DB_XREF=gi:3366801 /UG=Hs.285529 G protein-coupled receptor 49 /FL=gb:AF062006.1 gb:AF061444.1 gb:NM_003667.1	210393_at
hypothetical protein FLJ20048	gb:NM_017640.1 /DEF=Homo sapiens hypothetical protein FLJ20048 (FLJ20048), mRNA. /FEA=mRNA /GEN=FLJ20048 /PROD=hypothetical protein FLJ20048 /DB_XREF=gi:8923056 /UG=Hs.116470 hypothetical protein FLJ20048 /FL=gb:NM_017640.1	219573_at
cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2	gb:NM_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily IIJ (arachidonic acidepoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:NM_000775.1	205073_at
brain-specific protein p25 alpha	gb:NM_007030.1 /DEF=Homo sapiens brain-specific protein p25 alpha (p25), mRNA. /FEA=mRNA /GEN=p25 /PROD=brain-specific protein p25 alpha /DB_XREF=gi:5902017 /UG=Hs.29353 brain-specific protein p25 alpha	206179_s_at

	/FL=gb:AB017016.1 gb:NM_007030.1	
mucin 2, intestinal/trachea 1	gb:NM_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:NM_002457.1 gb:L21998.1	204673_at
hypothetical protein FLJ20174	gb:NM_017699.1 /DEF=Homo sapiens hypothetical protein FLJ20174 (FLJ20174), mRNA. /FEA=mRNA /GEN=FLJ20174 /PROD=hypothetical protein FLJ20174 /DB_XREF=gi:8923170 /UG=Hs.114556 hypothetical protein FLJ20174 /FL=gb:NM_017699.1	219734_at
metastasis-associated 1-like 1	gb:NM_004739.1 /DEF=Homo sapiens metastasis-associated 1-like 1 (MTA1L1), mRNA. /FEA=mRNA /GEN=MTA1L1 /PROD=metastasis-associated 1-like 1 /DB_XREF=gi:4758739 /UG=Hs.173043 metastasis-associated 1-like 1 /FL=gb:AB016591.1 gb:NM_004739.1 gb:AF295807.1	203444_s_at
bone morphogenetic protein 2	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
heparanase	gb:NM_006665.1 /DEF=Homo sapiens heparanase (HPSE), mRNA. /FEA=mRNA /GEN=HPSE /PROD=heparanase /DB_XREF=gi:5729872 /UG=Hs.44227 heparanase /FL=gb:AF165154.1 gb:AF152376.1 gb:NM_006665.1 gb:AF084467.1 gb:AF155510.1	219403_s_at
tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	gb:BC002794.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator), clone MGC:3753, mRNA, complete cds. /FEA=mRNA /PROD=tumor necrosis factor receptor superfamily,member 14 (herpesvirus entry mediator) /DB_XREF=gi:12803894 /UG=Hs.279899 tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) /FL=gb:BC002794.1 gb:U70321.1 gb:U81232.1 gb:NM_003820.1 gb:AF153978.1	209354_at
CUG triplet repeat, RNA-	Consensus includes gb:N36839 /FEA=EST /DB_XREF=gi:1157981	202156_s_at

binding protein 2	/DB_XREF=est:yy35f07.s1 /CLONE=IMAGE:273253 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	
ESTs, Moderately similar to AF078844 1 hqp0376 protein [H.sapiens]	Consensus includes gb:R06655 /FEA=EST /DB_XREF=gi:757275 /DB_XREF=est:yf10e02.r1 /CLONE=IMAGE:126458 /UG=Hs.188518 ESTs, Moderately similar to AF078844 1 hqp0376 protein H.sapiens	217546_at
hairless (mouse) homolog	gb:NM_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:NM_018411.1	220163_s_at
branched chain aminotransferase 1, cytosolic	Consensus includes gb:NM_005504.1 /DEF=Homo sapiens branched chain aminotransferase 1, cytosolic (BCAT1), mRNA. /FEA=CDS /GEN=BCAT1 /PROD=branched chain aminotransferase 1, cytosolic /DB_XREF=gi:5031606 /UG=Hs.157205 branched chain aminotransferase 1, cytosolic /FL=gb:U21551.1 gb:NM_005504.1	214452_at
pancreas-enriched phospholipase C	gb:NM_016341.1 /DEF=Homo sapiens pancreas-enriched phospholipase C (LOC51196), mRNA. /FEA=mRNA /GEN=LOC51196 /PROD=pancreas-enriched phospholipase C /DB_XREF=gi:7705940 /UG=Hs.6733 pancreas-enriched phospholipase C /FL=gb:AF190642.2 gb:AF117948.1 gb:NM_016341.1	205112_at
prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	gb:NM_000963.1 /DEF=Homo sapiens prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) (PTGS2), mRNA. /FEA=mRNA /GEN=PTGS2 /PROD=prostaglandin-endoperoxide synthase 2(prostaglandin GH synthase and cyclooxygenase) /DB_XREF=gi:4506264 /UG=Hs.196384 prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and	204748_at

	cyclooxygenase) /FL=gb:M90100.1 gb:L15326.1 gb:NM_000963.1	
phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	gb:NM_000314.1 /DEF=Homo sapiens phosphatase and tensin homolog (mutated in multiple advanced cancers 1) (PTEN), mRNA. /FEA=mRNA /GEN=PTEN /PROD=phosphatase and tensin homolog (mutated inmultiple advanced cancers 1) /DB_XREF=gi:4506248 /UG=Hs.10712 phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /FL=gb:U92436.1 gb:U93051.1 gb:U96180.1 gb:NM_000314.1	204054_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1 /CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	221872_at
protease inhibitor 3, skin-derived (SKALP)	gb:NM_002638.1 /DEF=Homo sapiens protease inhibitor 3, skin-derived (SKALP) (PI3), mRNA. /FEA=mRNA /GEN=PI3 /PROD=protease inhibitor 3, skin-derived (SKALP) /DB_XREF=gi:4505786 /UG=Hs.112341 protease inhibitor 3, skin-derived (SKALP) /FL=gb:NM_002638.1	203691_at
zinc finger protein 137 (clone pHZ-30)	gb:NM_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ-30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:NM_003438.1 gb:U09414.1	207394_at
myosin, light polypeptide 5, regulatory	gb:NM_002477.1 /DEF=Homo sapiens myosin, light polypeptide 5, regulatory (MYL5), mRNA. /FEA=mRNA /GEN=MYL5 /PROD=myosin, light polypeptide 5, regulatory /DB_XREF=gi:4505304 /UG=Hs.170482 myosin, light polypeptide 5, regulatory /FL=gb:L03785.1 gb:NM_002477.1	205145_s_at
tumor necrosis factor receptor superfamily, member 6	gb:NM_000043.1 /DEF=Homo sapiens tumor necrosis factor receptor superfamily, member 6 (TNFRSF6), mRNA. /FEA=mRNA /GEN=TNFRSF6 /PROD=apoptosis (APO-1) antigen 1 /DB_XREF=gi:4507582 /UG=Hs.82359 tumor necrosis factor receptor superfamily, member 6 /FL=gb:M67454.1 gb:NM_000043.1	204781_s_at
hypothetical	Consensus includes gb:AI339568 /FEA=EST	222727_s_at

protein FLJ22233	/DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	
regenerating gene type IV	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	Consensus includes gb:AK025615.1 /DEF=Homo sapiens cDNA: FLJ21962 fis, clone HEP05564. /FEA=mRNA /DB_XREF=gi:10438186 /UG=Hs.7567 Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	225285_at
phosphoprotein associated with glycosphingolipid-enriched microdomains	Consensus includes gb:AK000680.1 /DEF=Homo sapiens cDNA FLJ20673 fis, clone KAIA4464. /FEA=mRNA /DB_XREF=gi:7020924 /UG=Hs.266175 phosphoprotein associated with GEMs /FL=gb:AF240634.1 gb:NM_018440.1	225626_at
hypothetical protein FLJ20209	Consensus includes gb:BF111925 /FEA=EST /DB_XREF=gi:10941704 /DB_XREF=est:7l38g05.x1 /CLONE=IMAGE:3523784 /UG=Hs.3685 hypothetical protein FLJ20209	226171_at
Homo sapiens mRNA for KIAA1190 protein, partial cds	Consensus includes gb:AA532640 /FEA=EST /DB_XREF=gi:2276894 /DB_XREF=est:nj17c04.s1 /CLONE=IMAGE:986598 /UG=Hs.206259 Homo sapiens mRNA for KIAA1190 protein, partial cds	226484_at
KIAA1543 protein	Consensus includes gb:AB040976.1 /DEF=Homo sapiens mRNA for KIAA1543 protein, partial cds. /FEA=mRNA /GEN=KIAA1543 /PROD=KIAA1543 protein /DB_XREF=gi:7959352 /UG=Hs.17686 KIAA1543 protein	226494_at
hypothetical protein FLJ23563	Consensus includes gb:AW138767 /FEA=EST /DB_XREF=gi:6143085 /DB_XREF=est:UI-H-BI1-aep-a-12-0-UI.s1 /CLONE=IMAGE:2719799 /UG=Hs.274256 hypothetical protein FLJ23563	227180_at
ESTs	Consensus includes gb:AW264333 /FEA=EST /DB_XREF=gi:6641075 /DB_XREF=est:xq98e01.x1	227320_at

	/CLONE=IMAGE:2758680 /UG=Hs.21835 ESTs	
ESTs	Consensus includes gb:BF589359 /FEA=EST /DB_XREF=gi:11681683 /DB_XREF=est:nab25d01.x1 /CLONE=IMAGE:3266737 /UG=Hs.13256 ESTs	227354_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:3852062, mRNA, complete cds	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
ESTs	Consensus includes gb:AI700341 /FEA=EST /DB_XREF=gi:4988241 /DB_XREF=est:wd06e10.x1 /CLONE=IMAGE:2327370 /UG=Hs.110406 ESTs	228653_at
ESTs	Consensus includes gb:BG494007 /FEA=EST /DB_XREF=gi:13455521 /DB_XREF=est:602542289F1 /CLONE=IMAGE:4673182 /UG=Hs.203213 ESTs	228716_at
ESTs	Consensus includes gb:AI559300 /FEA=EST /DB_XREF=gi:4509505 /DB_XREF=est:tq43d03.x1 /CLONE=IMAGE:2211557 /UG=Hs.294140 ESTs	229331_at
hypothetical protein	Consensus includes gb:AI830823 /FEA=EST /DB_XREF=gi:5451416 /DB_XREF=est:wj52b06.x1 /CLONE=IMAGE:2406419 /UG=Hs.95549 hypothetical protein	229439_s_at
ESTs	Consensus includes gb:BF431989 /FEA=EST /DB_XREF=gi:11444103 /DB_XREF=est:nab84a05.x1 /CLONE=IMAGE:3274280 /UG=Hs.203213 ESTs	229657_at
ESTs	Consensus includes gb:BF589413 /FEA=EST	229893_at

	/DB_XREF=gi:11681737 /DB_XREF=est:nab26b11.x1 /CLONE=IMAGE:3267020 /UG=Hs.55501 ESTs	
brain-specific protein p25 alpha	Consensus includes gb:BG055052 /FEA=EST /DB_XREF=gi:12512386 /DB_XREF=est:nac94g06.x1 /CLONE=IMAGE:3441995 /UG=Hs.29353 brain-specific protein p25 alpha	230104_s_at
ESTs, Weakly similar to MMHUE4 erythrocyte membrane protein 4.1, parent splice form [H.sapiens]	Consensus includes gb:BF110588 /FEA=EST /DB_XREF=gi:10940278 /DB_XREF=est:7n39e12.x1 /CLONE=IMAGE:3567071 /UG=Hs.150478 ESTs, Weakly similar to KIAA0987 protein H.sapiens	230645_at
ESTs	Consensus includes gb:BF592062 /FEA=EST /DB_XREF=gi:11684386 /DB_XREF=est:7n98h06.x1 /CLONE=IMAGE:3572962 /UG=Hs.233890 ESTs	230760_at
hepatocyte nuclear factor 4, alpha	Consensus includes gb:AI032108 /FEA=EST /DB_XREF=gi:3250320 /DB_XREF=est:ow92d11.x1 /CLONE=IMAGE:1654293 /UG=Hs.54424 hepatocyte nuclear factor 4, alpha	230914_at
ESTs	Consensus includes gb:AW203959 /FEA=EST /DB_XREF=gi:6503431 /DB_XREF=est:UI-H-BI1-aeu-b-12-0-UI.s1 /CLONE=IMAGE:2720590 /UG=Hs.149532 ESTs	230944_at
ESTs	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376 ESTs	231148_at
hypothetical protein FLJ23045	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at

Homo sapiens PAC clone RP5-855D21	Consensus includes gb:AC004908 /DEF=Homo sapiens PAC clone RP5-855D21 /FEA=CDS_3 /DB_XREF=gi:4156179 /UG=Hs.249181 Homo sapiens PAC clone RP5-855D21	232641_at
putative microtubule-binding protein	Consensus includes gb:AJ251708.1 /DEF=Homo sapiens partial mRNA for putative microtubule-binding protein. /FEA=mRNA /PROD=putative microtubule-binding protein /DB_XREF=gi:6491740 /UG=Hs.326544 putative microtubule-binding protein	234669_x_at
ESTs	Consensus includes gb:AI741469 /FEA=EST /DB_XREF=gi:5109757 /DB_XREF=est:wg11b01.x1 /CLONE=IMAGE:2364745 /UG=Hs.57787 ESTs	234970_at
ESTs	Consensus includes gb:AI417897 /FEA=EST /DB_XREF=gi:4261401 /DB_XREF=est:tg55b06.x1 /CLONE=IMAGE:2112659 /UG=Hs.235860 ESTs	235444_at
ESTs	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
ESTs	Consensus includes gb:AV741130 /FEA=EST /DB_XREF=gi:10858711 /DB_XREF=est:AV741130 /CLONE=CBCATB06 /UG=Hs.173704 ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens	235651_at
ESTs	Consensus includes gb:AW339510 /FEA=EST /DB_XREF=gi:6836136 /DB_XREF=est:xz91h08.x1 /CLONE=IMAGE:2871615 /UG=Hs.42722 ESTs	235866_at
ESTs	Consensus includes gb:AI076192 /FEA=EST /DB_XREF=gi:3405370 /DB_XREF=est:oz01g07.x1 /CLONE=IMAGE:1674108 /UG=Hs.131933 ESTs	236422_at
ESTs	Consensus includes gb:AL044570 /FEA=EST /DB_XREF=gi:5432785 /DB_XREF=est:DKFZp434L082_s1 /CLONE=DKFZp434L082 /UG=Hs.147975 ESTs	236548_at

ESTs	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
Homo sapiens, clone MGC:16402 IMAGE:3940360, mRNA, complete cds	Consensus includes gb:T69015 /FEA=EST /DB_XREF=gi:680163 /DB_XREF=est:yc31f04.s1 /CLONE=IMAGE:82303 /UG=Hs.192728 ESTs	238422_at
ESTs	Consensus includes gb:AA502384 /FEA=EST /DB_XREF=gi:2237351 /DB_XREF=est:ne27f11.s1 /CLONE=IMAGE:898605 /UG=Hs.151529 ESTs	238956_at
ESTs	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at
ESTs	Consensus includes gb:AA088446 /FEA=EST /DB_XREF=gi:1633958 /DB_XREF=est:zl89f04.s1 /CLONE=IMAGE:511807 /UG=Hs.170298 ESTs	239065_at
ESTs	Consensus includes gb:AI493046 /FEA=EST /DB_XREF=gi:4394049 /DB_XREF=est:qz49b04.x1 /CLONE=IMAGE:2030191 /UG=Hs.146133 ESTs	239148_at
ESTs	Consensus includes gb:AI243098 /FEA=EST /DB_XREF=gi:3838495 /DB_XREF=est:qh26e03.x1 /CLONE=IMAGE:1845820 /UG=Hs.178398 ESTs	239966_at
ESTs, Weakly similar to A49175 Motch B protein - mouse [M.musculus]	Consensus includes gb:AI633523 /FEA=EST /DB_XREF=gi:4684853 /DB_XREF=est:th68b11.x1 /CLONE=IMAGE:2123805 /UG=Hs.44705 ESTs	240106_at
betacellulin	Consensus includes gb:AI620677 /FEA=EST /DB_XREF=gi:4629803 /DB_XREF=est:tu85e09.x1 /CLONE=IMAGE:2257864 /UG=Hs.154191 ESTs	241412_at
ESTs	Consensus includes gb:BF696216 /FEA=EST /DB_XREF=gi:11981624	242626_at

	/DB_XREF=est:602124536F1 /CLONE=IMAGE:4281632 /UG=Hs.188724 ESTs	
ESTs	Consensus includes gb:N57929 /FEA=EST /DB_XREF=gi:1201819 /DB_XREF=est:yv61e06.s1 /CLONE=IMAGE:247234 /UG=Hs.48100 ESTs	242978_x_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY [H.sapiens]	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
ESTs	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at

The two biomarker probe sets A and B were then combined, a total of 161 different probe sets, and the redundant polynucleotides were removed, representing 125 unique polynucleotides which are provided below in Table 4. The Table 4 polynucleotides are biomarkers of the invention.

TABLE 4 - Biomarkers

Unigene Title And SEQ ID NO:	Affymetrix Description	Affymetrix probe set
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) SEQ ID NOS: 1 (DNA) and 126 (amino acid)	gb:NM_005518.1 /DEF=Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) (HMGCS2), mRNA. /FEA=mRNA /GEN=HMGCS2 /PROD=3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2(mitochondrial) /DB_XREF=gi:5031750 /UG=Hs.59889 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) /FL=gb:NM_005518.1	204607_at
ATPase, Class V, type 10B	Consensus includes gb:AW006935 /FEA=EST /DB_XREF=gi:5855713 /DB_XREF=est:wt08b11.x1	214070_s_at

SEQ ID NO: 2 (DNA)	/CLONE=IMAGE:2506845 /UG=Hs.109358 ATPase, Class V, type 10B	
bone morphogenetic protein 2 SEQ ID NOS: 3 (DNA) and 127 (amino acid)	gb:NM_001200.1 /DEF=Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA. /FEA=mRNA /GEN=BMP2 /PROD=bone morphogenetic protein 2 precursor /DB_XREF=gi:4557368 /UG=Hs.73853 bone morphogenetic protein 2 /FL=gb:NM_001200.1	205290_s_at
brain-specific protein p25 alpha SEQ ID NOS: 4 (DNA) and 128 (amino acid)	gb:NM_007030.1 /DEF=Homo sapiens brain-specific protein p25 alpha (p25), mRNA. /FEA=mRNA /GEN=p25 /PROD=brain-specific protein p25 alpha /DB_XREF=gi:5902017 /UG=Hs.29353 brain-specific protein p25 alpha /FL=gb:AB017016.1 gb:NM_007030.1	206179_s_at
branched chain aminotransferase 1, cytosolic SEQ ID NOS: 5 (DNA) and 129 (amino acid)	Consensus includes gb:NM_005504.1 /DEF=Homo sapiens branched chain aminotransferase 1, cytosolic (BCAT1), mRNA. /FEA=CDS /GEN=BCAT1 /PROD=branched chain aminotransferase 1, cytosolic /DB_XREF=gi:5031606 /UG=Hs.157205 branched chain aminotransferase 1, cytosolic /FL=gb:U21551.1 gb:NM_005504.1	214452_at
BTG family, member 2 SEQ ID NOS: 6 (DNA) and 130 (amino acid)	gb:NM_006763.1 /DEF=Homo sapiens BTG family, member 2 (BTG2), mRNA. /FEA=mRNA /GEN=BTG2 /PROD=BTG family, member 2 /DB_XREF=gi:5802987 /UG=Hs.75462 BTG family, member 2 /FL=gb:U72649.1 gb:NM_006763.1	201236_s_at
Carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) SEQ ID NOS: 7 (DNA) and 131 (amino acid)	gb:BC005008.1 /DEF=Homo sapiens, carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen), clone MGC:10467, mRNA, complete cds. /FEA=mRNA /PROD=carcinoembryonic antigen-related cell adhesionmolecule 6 (non-specific cross reacting antigen) /DB_XREF=gi:13477106 /UG=Hs.73848 carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) /FL=gb:BC005008.1 gb:M18216.1 gb:M29541.1 gb:NM_002483.1	203757_s_at
caspase 10, apoptosis-related cysteine protease SEQ ID NOS: 8	gb:NM_001230.1 /DEF=Homo sapiens caspase 10, apoptosis-related cysteine protease (CASP10), mRNA. /FEA=mRNA /GEN=CASP10 /PROD=caspase 10, apoptosis-related cysteine protease	205467_at

(DNA) and 132 (amino acid)	/DB_XREF=gi:4502568 /UG=Hs.5353 caspase 10, apoptosis-related cysteine protease /FL=gb:U60519.1 gb:NM_001230.1	
CUG triplet repeat, RNA-binding protein 2 SEQ ID NOS: 9 (DNA) and 133 (amino acid)	gb:NM_006561.1 /DEF=Homo sapiens CUG triplet repeat, RNA-binding protein 2 (CUGBP2), mRNA. /FEA=mRNA /GEN=CUGBP2 /PROD=CUG triplet repeat, RNA-binding protein 2 /DB_XREF=gi:5729815 /UG=Hs.211610 CUG triplet repeat, RNA-binding protein 2 /FL=gb:U69546.1 gb:AF036956.1 gb:AF090694.1 gb:NM_006561.1	202158_s_at
cystatin S SEQ ID NOS: 10 (DNA) and 134 (amino acid)	gb:NM_001899.1 /DEF=Homo sapiens cystatin S (CST4), mRNA. /FEA=mRNA /GEN=CST4 /PROD=cystatin S /DB_XREF=gi:4503108 /UG=Hs.56319 cystatin S /FL=gb:NM_001899.1	206994_at
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) SEQ ID NOS: 11 (DNA) and 135 (amino acid)	gb:NM_000492.2 /DEF=Homo sapiens cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) (CFTR), mRNA. /FEA=mRNA /GEN=CFTR /PROD=cystic fibrosis transmembrane conductanceregulator, ATP-binding cassette (sub-family C, member 7) /DB_XREF=gi:6995995 /UG=Hs.663 cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) /FL=gb:NM_000492.2	205043_at
cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 SEQ ID NOS: 12 (DNA) and 136 (amino acid)	gb:NM_000775.1 /DEF=Homo sapiens cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 (CYP2J2), mRNA. /FEA=mRNA /GEN=CYP2J2 /PROD=cytochrome P450, subfamily IIJ (arachidonic acidepoxygenase) polypeptide 2 /DB_XREF=gi:4503226 /UG=Hs.152096 cytochrome P450, subfamily IIJ (arachidonic acid epoxygenase) polypeptide 2 /FL=gb:U37143.1 gb:NM_000775.1	205073_at
dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) SEQ ID NOS 13 (DNA) and 137 (amino acid)	gb:M80536.1 /DEF=H.sapiens dipeptidyl peptidase IV (DPP4) mRNA, complete cds. /FEA=mRNA /GEN=DPP4 /PROD=dipeptidyl peptidase IV /DB_XREF=gi:181569 /UG=Hs.44926 dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2) /FL=gb:M80536.1 gb:NM_001935.1	203716_s_at
DKFZP434C091 protein	Consensus includes gb:AL080170.1 /DEF=Homo sapiens mRNA; cDNA	215047_at

SEQ ID NO: 14 (DNA)	DKFZp434C091 (from clone DKFZp434C091); partial cds. /FEA=mRNA /GEN=DKFZp434C091 /PROD=hypothetical protein /DB_XREF=gi:5262639 /UG=Hs.51692 DKFZP434C091 protein	
dopa decarboxylase (aromatic L-amino acid decarboxylase) SEQ ID NO: 15 (DNA)	Consensus includes gb:AW772056 /FEA=EST /DB_XREF=gi:7704118 /DB_XREF=est:hn64g06.x1 /CLONE=IMAGE:3032698 /UG=Hs.150403 dopa decarboxylase (aromatic L-amino acid decarboxylase)	214347_s_at
EphA1 SEQ ID NOS: 16 (DNA) and 138 (amino acid)	gb:NM_005232.1 /DEF=Homo sapiens EphA1 (EPHA1), mRNA. /FEA=mRNA /GEN=EPHA1 /PROD=EphA1 /DB_XREF=gi:4885208 /UG=Hs.89839 EphA1 /FL=gb:M18391.1 gb:NM_005232.1	205977_s_at
ESTs, Moderately similar to AF078844 1 hqp0376 protein [H.sapiens] SEQ ID NO: 17 (DNA)	Consensus includes gb:R06655 /FEA=EST /DB_XREF=gi:757275 /DB_XREF=est:yf10e02.r1 /CLONE=IMAGE:126458 /UG=Hs.188518 ESTs, Moderately similar to AF078844 1 hqp0376 protein H.sapiens	217546_at
ESTs, Weakly similar to I38022 hypothetical protein [H.sapiens] SEQ ID NO: 18 (DNA)	Consensus includes gb:AW675655 /FEA=EST /DB_XREF=gi:7540890 /DB_XREF=est:ba52e01.x1 /CLONE=IMAGE:2900184 /UG=Hs.314158 ESTs	222354_at
fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) SEQ ID NOS: 19 (DNA) and 139 (amino acid)	gb:NM_022969.1 /DEF=Homo sapiens fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) (FGFR2), transcript variant 2, mRNA. /FEA=mRNA /GEN=FGFR2 /PROD=fibroblast growth factor receptor 2, isoform 2precursor /DB_XREF=gi:13186252 /UG=Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome) /FL=gb:NM_022969.1 gb:M97193.1 gb:M80634.1	203638_s_at
FXYD domain-containing ion	gb:BC005238.1 /DEF=Homo sapiens, FXYD domain-containing ion transport regulator 3,	202489_s_at

transport regulator 3 SEQ ID NOS: 20 (DNA) and 140 (amino acid)	clone MGC:12265, mRNA, complete cds. /FEA=mRNA /PROD=FXYD domain-containing ion transport regulator3 /DB_XREF=gi:13528881 /UG=Hs.301350 FXYD domain-containing ion transport regulator 3 /FL=gb:NM_005971.2 gb:BC005238.1	
G protein-coupled receptor 49 SEQ ID NOS: 21 (DNA) and 141 (amino acid)	gb:AF062006.1 /DEF=Homo sapiens orphan G protein-coupled receptor HG38 mRNA, complete cds. /FEA=mRNA /PROD=orphan G protein-coupled receptor HG38 /DB_XREF=gi:3366801 /UG=Hs.285529 G protein-coupled receptor 49 /FL=gb:AF062006.1 gb:AF061444.1 gb:NM_003667.1	210393_at
hairless (mouse) homolog SEQ ID NOS: 22 (DNA) and 142 (amino acid)	gb:NM_018411.1 /DEF=Homo sapiens hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) (HSA277165), mRNA. /FEA=mRNA /GEN=HSA277165 /PROD=hairless protein /DB_XREF=gi:11036651 /UG=Hs.272367 hairless protein (putative single zinc finger transcription factor protein, responsible for autosomal recessive universal congenital alopecia, HR gene) /FL=gb:NM_018411.1	220163_s_at
hemoglobin, alpha 1 SEQ ID NOS: 23 (DNA) and 143 (amino acid)	gb:BC005931.1 /DEF=Homo sapiens, hemoglobin, alpha 2, clone MGC:14541, mRNA, complete cds. /FEA=mRNA /PROD=hemoglobin, alpha 2 /DB_XREF=gi:13543547 /FL=gb:BC005931.1	211745_x_at
hemoglobin, alpha 2 SEQ ID NO: 24 (DNA)	Consensus includes gb:T50399 /FEA=EST /DB_XREF=gi:652259 /DB_XREF=est:yb30b11.s1 /CLONE=IMAGE:72669 /UG=Hs.251577 hemoglobin, alpha 1	214414_x_at
heparanase SEQ ID NOS: 25 (DNA) and 144 (amino acid)	gb:NM_006665.1 /DEF=Homo sapiens heparanase (HPSE), mRNA. /FEA=mRNA /GEN=HPSE /PROD=heparanase /DB_XREF=gi:5729872 /UG=Hs.44227 heparanase /FL=gb:AF165154.1 gb:AF152376.1 gb:NM_006665.1 gb:AF084467.1 gb:AF155510.1	219403_s_at
Hermansky-Pudlak syndrome	Consensus includes gb:AL022313 /DEF=Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3	217354_s_at

SEQ ID NOS: 26 (DNA) and 145 (amino acid)	Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene f... /FEA=CDS_3 /DB_XREF=gi:4200326 /UG=Hs.272270 Human DNA sequence from clone RP5-1119A7 on chromosome 22q12.2-12.3 Contains the TXN2 gene for mitochondrial thioredoxin, a novel gene, the EIF3S7 gene for eukaryotic translation initiation factor 3 subunit 7 (zeta, 6667kD) (EIF3-P66), the gene for a nov	
HERV-H LTR-associating 2 SEQ ID NOS: 27 (DNA) and 146 (amino acid)	gb:NM_007072.1 /DEF=Homo sapiens HERV-H LTR-associating 2 (HHLA2), mRNA. /FEA=mRNA /GEN=HHLA2 /PROD=HERV-H LTR-associating 2 /DB_XREF=gi:5901963 /UG=Hs.252351 HERV-H LTR-associating 2 /FL=gb:AF126162.1 gb:NM_007072.1	220812_s_at
Homo sapiens clone 24707 mRNA sequence SEQ ID NO: 28 (DNA)	Consensus includes gb:AW593996 /FEA=EST /DB_XREF=gi:7281254 /DB_XREF=est:hg41g06.x1 /CLONE=IMAGE:2948218 /UG=Hs.124969 Homo sapiens clone 24707 mRNA sequence	213256_at
Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042) SEQ ID NO: 29 (DNA)	Consensus includes gb:AL049983.1 /DEF=Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042). /FEA=mRNA /DB_XREF=gi:4884234 /UG=Hs.240136 Homo sapiens mRNA; cDNA DKFZp564D042 (from clone DKFZp564D042)	217288_at
hypothetical protein FLJ20048 SEQ ID NOS: 30 (DNA) and 147 (amino acid)	gb:NM_017640.1 /DEF=Homo sapiens hypothetical protein FLJ20048 (FLJ20048), mRNA. /FEA=mRNA /GEN=FLJ20048 /PROD=hypothetical protein FLJ20048 /DB_XREF=gi:8923056 /UG=Hs.116470 hypothetical protein FLJ20048 /FL=gb:NM_017640.1	219573_at
hypothetical protein FLJ20075 SEQ ID NOS: 31 (DNA) and 148 (amino acid)	gb:NM_017655.1 /DEF=Homo sapiens hypothetical protein FLJ20075 (FLJ20075), mRNA. /FEA=mRNA /GEN=FLJ20075 /PROD=hypothetical protein FLJ20075 /DB_XREF=gi:8923083 /UG=Hs.205058 hypothetical protein FLJ20075 /FL=gb:NM_017655.1	219970_at

interferon consensus sequence binding protein 1 SEQ ID NO: 32 (DNA)	Consensus includes gb:AI073984 /FEA=EST /DB_XREF=gi:3400628 /DB_XREF=est:oy66c05.x1 /CLONE=IMAGE:1670792 /UG=Hs.14453 interferon consensus sequence binding protein 1 /FL=gb:M91196.1 gb:NM_002163.1	204057_at
KIAA0690 protein SEQ ID NO: 33 (DNA)	Consensus includes gb:AK000238.1 /DEF=Homo sapiens cDNA FLJ20231 fis, clone COLF5511, highly similar to AB014590 Homo sapiens mRNA for KIAA0690 protein. /FEA=mRNA /DB_XREF=gi:7020188 /UG=Hs.60103 KIAA0690 protein	216360_x_at
matrilin 3 SEQ ID NOS: 34 (DNA) and 149 (amino acid)	gb:NM_002381.2 /DEF=Homo sapiens matrilin 3 (MATN3) precursor, mRNA. /FEA=mRNA /GEN=MATN3 /PROD=matrilin 3 precursor /DB_XREF=gi:13518040 /UG=Hs.278461 matrilin 3 /FL=gb:NM_002381.2	206091_at
metastasis-associated 1-like 1 SEQ ID NOS: 35 (DNA) and 150 (amino acid)	gb:NM_004739.1 /DEF=Homo sapiens metastasis-associated 1-like 1 (MTA1L1), mRNA. /FEA=mRNA /GEN=MTA1L1 /PROD=metastasis-associated 1-like 1 /DB_XREF=gi:4758739 /UG=Hs.173043 metastasis-associated 1-like 1 /FL=gb:AB016591.1 gb:NM_004739.1 gb:AF295807.1	203444_s_at
mucin 2, intestinal/tracheal SEQ ID NOS: 36 (DNA) and 151 (amino acid)	gb:NM_002457.1 /DEF=Homo sapiens mucin 2, intestinaltracheal (MUC2), mRNA. /FEA=mRNA /GEN=MUC2 /PROD=mucin 2, intestinaltracheal /DB_XREF=gi:4505284 /UG=Hs.315 mucin 2, intestinaltracheal /FL=gb:NM_002457.1 gb:L21998.1	204673_at
mucin 3B SEQ ID NOS: 37 (DNA) and 152 (amino acid)	Consensus includes gb:AB038783.1 /DEF=Homo sapiens MUC3B mRNA for intestinal mucin, partial cds. /FEA=mRNA /GEN=MUC3B /PROD=intestinal mucin /DB_XREF=gi:9929917 /UG=Hs.129782 mucin 3A, intestinal	214898_x_at
myosin, heavy polypeptide 13, skeletal muscle SEQ ID NOS: 38 (DNA) and 153 (amino acid)	gb:NM_003802.1 /DEF=Homo sapiens myosin, heavy polypeptide 13, skeletal muscle (MYH13), mRNA. /FEA=mRNA /GEN=MYH13 /PROD=myosin, heavy polypeptide 13, skeletal muscle /DB_XREF=gi:11321578 /UG=Hs.278488 myosin, heavy polypeptide 13, skeletal muscle /FL=gb:NM_003802.1 gb:AF111782.2	208208_at

myosin, light polypeptide 5, regulatory SEQ ID NOS: 39 (DNA) and 154 (amino acid)	gb:NM_002477.1 /DEF=Homo sapiens myosin, light polypeptide 5, regulatory (MYL5), mRNA. /FEA=mRNA /GEN=MYL5 /PROD=myosin, light polypeptide 5, regulatory /DB_XREF=gi:4505304 /UG=Hs.170482 myosin, light polypeptide 5, regulatory /FL=gb:L03785.1 gb:NM_002477.1	205145_s_at
nuclear receptor subfamily 3, group C, member 2 SEQ ID NOS: 40 (DNA) and 155 (amino acid)	gb:NM_000901.1 /DEF=Homo sapiens nuclear receptor subfamily 3, group C, member 2 (NR3C2), mRNA. /FEA=mRNA /GEN=NR3C2 /PROD=nuclear receptor subfamily 3, group C, member 2 /DB_XREF=gi:4505198 /UG=Hs.1790 nuclear receptor subfamily 3, group C, member 2 /FL=gb:M16801.1 gb:NM_000901.1	205259_at
nuclear receptor subfamily 5, group A, member 2 SEQ ID NOS: 41 (DNA) and 156 (amino acid)	Consensus includes gb:AF228413.1 /DEF=Homo sapiens hepatocyte transcription factor mRNA, 3UTR. /FEA=mRNA /DB_XREF=gi:7677372 /UG=Hs.183123 nuclear receptor subfamily 5, group A, member 2 /FL=gb:U93553.1 gb:AB019246.1 gb:AF124247.1	210174_at
pancreas-enriched phospholipase C SEQ ID NOS: 42 (DNA) and 157 (amino acid)	gb:NM_016341.1 /DEF=Homo sapiens pancreas-enriched phospholipase C (LOC51196), mRNA. /FEA=mRNA /GEN=LOC51196 /PROD=pancreas-enriched phospholipase C /DB_XREF=gi:7705940 /UG=Hs.6733 pancreas-enriched phospholipase C /FL=gb:AF190642.2 gb:AF117948.1 gb:NM_016341.1	205112_at
peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase SEQ ID NOS: 43 (DNA) and 158 (amino acid)	gb:NM_018441.1 /DEF=Homo sapiens peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase (HSA250303), mRNA. /FEA=mRNA /GEN=HSA250303 /PROD=peroxisomal trans 2-enoyl CoA reductase;putative short chain alcohol dehydrogenase /DB_XREF=gi:8923751 /UG=Hs.281680 peroxisomal trans 2-enoyl CoA reductase; putative short chain alcohol dehydrogenase /FL=gb:NM_018441.1	221142_s_at
phosducin SEQ ID NOS: 44 (DNA) and 159 (amino acid)	gb:M33478.1 /DEF=Human 33-kDa phototransducing protein mRNA, complete cds. /FEA=mRNA /DB_XREF=gi:177186 /UG=Hs.550 phosducin /FL=gb:NM_022577.1 gb:M33478.1	211496_s_at

	gb:AF076465.1	
phosphatase and tensin homolog (mutated in multiple advanced cancers 1) SEQ ID NOS: 45 (DNA) and 160 (amino acid)	gb:NM_000314.1 /DEF=Homo sapiens phosphatase and tensin homolog (mutated in multiple advanced cancers 1) (PTEN), mRNA. /FEA=mRNA /GEN=PTEN /PROD=phosphatase and tensin homolog (mutated inmultiple advanced cancers 1) /DB_XREF=gi:4506248 /UG=Hs.10712 phosphatase and tensin homolog (mutated in multiple advanced cancers 1) /FL=gb:U92436.1 gb:U93051.1 gb:U96180.1 gb:NM_000314.1	204054_at
potassium channel, subfamily K, member 1 (TWIK-1) SEQ ID NOS: 46 (DNA) and 161 (amino acid)	gb:U90065.1 /DEF=Human potassium channel KCNO1 mRNA, complete cds. /FEA=mRNA /PROD=potassium channel KCNO1 /DB_XREF=gi:1916294 /UG=Hs.79351 potassium channel, subfamily K, member 1 (TWIK-1) /FL=gb:U33632.1 gb:U90065.1 gb:U76996.1 gb:NM_002245.1	204678_s_at
prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) SEQ ID NOS: 47 (DNA) and 162 (amino acid)	gb:NM_000963.1 /DEF=Homo sapiens prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) (PTGS2), mRNA. /FEA=mRNA /GEN=PTGS2 /PROD=prostaglandin-endoperoxide synthase 2(prostaglandin GH synthase and cyclooxygenase) /DB_XREF=gi:4506264 /UG=Hs.196384 prostaglandin-endoperoxide synthase 2 (prostaglandin GH synthase and cyclooxygenase) /FL=gb:M90100.1 gb:L15326.1 gb:NM_000963.1	204748_at
protease inhibitor 3, skin-derived (SKALP) SEQ ID NOS: 48 (DNA) and 163 (amino acid)	gb:NM_002638.1 /DEF=Homo sapiens protease inhibitor 3, skin-derived (SKALP) (PI3), mRNA. /FEA=mRNA /GEN=PI3 /PROD=protease inhibitor 3, skin-derived (SKALP) /DB_XREF=gi:4505786 /UG=Hs.112341 protease inhibitor 3, skin-derived (SKALP) /FL=gb:NM_002638.1	203691_at
PTPRF interacting protein, binding protein 2 (liprin beta 2) SEQ ID NO: 49 (DNA)	Consensus includes gb:AI692180 /FEA=EST /DB_XREF=gi:4969520 /DB_XREF=est:wd37f06.x1 /CLONE=IMAGE:2330339 /UG=Hs.12953 PTPRF interacting protein, binding protein 2 (liprin beta 2)	212841_s_at
retinoic acid receptor responder (tazarotene induced) 1	Consensus includes gb:AI669229 /FEA=EST /DB_XREF=gi:4834003 /DB_XREF=est:wc13e06.x1	221872_at

SEQ ID NO: 50 (DNA)	/CLONE=IMAGE:2315074 /UG=Hs.82547 retinoic acid receptor responder (tazarotene induced) 1	
Rho GTPase activating protein 8 SEQ ID NOS: 51 (DNA) and 164 (amino acid)	gb:NM_015366.1 /DEF=Homo sapiens Rho GTPase activating protein 8 (ARHGAP8), mRNA. /FEA=mRNA /GEN=ARHGAP8 /PROD=Rho GTPase activating protein 8 /DB_XREF=gi:7656903 /UG=Hs.102336 Rho GTPase activating protein 8 /FL=gb:NM_015366.1	205980_s_at
ribonuclease, RNase A family, 1 (pancreatic) SEQ ID NOS: 52 (DNA) and 165 (amino acid)	gb:NM_002933.1 /DEF=Homo sapiens ribonuclease, RNase A family, 1 (pancreatic) (RNASE1), mRNA. /FEA=mRNA /GEN=RNASE1 /PROD=ribonuclease, RNase A family, 1 (pancreatic) /DB_XREF=gi:4506546 /UG=Hs.78224 ribonuclease, RNase A family, 1 (pancreatic) /FL=gb:BC005324.1 gb:NM_002933.1 gb:D26129.1	201785_at
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 SEQ ID NOS: 53 (DNA) and 166 (amino acid)	gb:NM_002639.1 /DEF=Homo sapiens serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5), mRNA. /FEA=mRNA /GEN=SERPINB5 /PROD=serine (or cysteine) proteinase inhibitor, cladeB (ovalbumin), member 5 /DB_XREF=gi:4505788 /UG=Hs.55279 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 /FL=gb:NM_002639.1 gb:U04313.1	204855_at
spondin 1, (f-spondin) extracellular matrix protein SEQ ID NO: 54 (DNA)	Consensus includes gb:AI885290 /FEA=EST /DB_XREF=gi:5590454 /DB_XREF=est:wl92a04.x1 /CLONE=IMAGE:2432334 /UG=Hs.5378 spondin 1, (f-spondin) extracellular matrix protein	213994_s_at
superoxide dismutase 3, extracellular SEQ ID NOS: 55 (DNA) and 167 (amino acid)	gb:NM_003102.1 /DEF=Homo sapiens superoxide dismutase 3, extracellular (SOD3), mRNA. /FEA=mRNA /GEN=SOD3 /PROD=superoxide dismutase 3, extracellular /DB_XREF=gi:4507150 /UG=Hs.2420 superoxide dismutase 3, extracellular /FL=gb:J02947.1 gb:NM_003102.1	205236_x_at
tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	gb:BC002794.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator), clone MGC:3753, mRNA, complete cds. /FEA=mRNA /PROD=tumor necrosis factor receptor superfamily,member 14 (herpesvirus	209354_at

SEQ ID NOS: 56 (DNA) and 168 (amino acid)	entry mediator) /DB_XREF=gi:12803894 /UG=Hs.279899 tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) /FL=gb:BC002794.1 gb:U70321.1 gb:U81232.1 gb:NM_003820.1 gb:AF153978.1	
tumor necrosis factor receptor superfamily, member 6 SEQ ID NOS: 57 (DNA) and 169 (amino acid)	gb:NM_000043.1 /DEF=Homo sapiens tumor necrosis factor receptor superfamily, member 6 (TNFRSF6), mRNA. /FEA=mRNA /GEN=TNFRSF6 /PROD=apoptosis (APO-1) antigen 1 /DB_XREF=gi:4507582 /UG=Hs.82359 tumor necrosis factor receptor superfamily, member 6 /FL=gb:M67454.1 gb:NM_000043.1	204781_s_at
zinc finger protein 137 (clone pHZ-30) SEQ ID NOS: 58 (DNA) and 170 (amino acid)	gb:NM_003438.1 /DEF=Homo sapiens zinc finger protein 137 (clone pHZ-30) (ZNF137), mRNA. /FEA=mRNA /GEN=ZNF137 /PROD=zinc finger protein 137 (clone pHZ-30) /DB_XREF=gi:4507988 /UG=Hs.151689 zinc finger protein 137 (clone pHZ-30) /FL=gb:NM_003438.1 gb:U09414.1	207394_at
hypothetical protein FLJ22233 SEQ ID NO: 59 (DNA)	Consensus includes gb:AI339568 /FEA=EST /DB_XREF=gi:4076495 /DB_XREF=est:qk67e10.x1 /CLONE=IMAGE:1874058 /UG=Hs.286194 hypothetical protein FLJ22233 /FL=gb:NM_024959.1	222727_s_at
regenerating gene type IV SEQ ID NOS: 60 (DNA) and 171 (amino acid)	gb:AY007243.1 /DEF=Homo sapiens regenerating gene type IV mRNA, complete cds. /FEA=mRNA /PROD=regenerating gene type IV /DB_XREF=gi:12621025 /UG=Hs.105484 Homo sapiens regenerating gene type IV mRNA, complete cds /FL=gb:AY007243.1	223447_at
Homo sapiens cDNA: FLJ21962 fis, clone HEP05564 SEQ ID NO: 61 (DNA)	Consensus includes gb:AK025615.1 /DEF=Homo sapiens cDNA: FLJ21962 fis, clone HEP05564. /FEA=mRNA /DB_XREF=gi:10438186 /UG=Hs.7567 Homo sapiens cDNA: FLJ21962 fis, clone HEP05564	225285_at
ESTs SEQ ID NO: 62 (DNA)	Consensus includes gb:N37023 /FEA=EST /DB_XREF=gi:1158165 /DB_XREF=est:yy40d03.s1 /CLONE=IMAGE:273701 /UG=Hs.235883 ESTs	225407_at
phosphoprotein associated with glycosphingolipid-	Consensus includes gb:AK000680.1 /DEF=Homo sapiens cDNA FLJ20673 fis, clone KAIA4464. /FEA=mRNA	225626_at

enriched microdomains SEQ ID NOS: 63 (DNA) and 172 (amino acid)	/DB_XREF=gi:7020924 /UG=Hs.266175 phosphoprotein associated with GEMs /FL=gb:AF240634.1 gb:NM_018440.1	
prostate cancer associated protein 7 SEQ ID NO: 64 (DNA)	Consensus includes gb:AA633076 /FEA=EST /DB_XREF=gi:2556490 /DB_XREF=est:nq38a06.s1 /CLONE=IMAGE:1146130 /UG=Hs.27495 prostate cancer associated protein 7	226167_at
Homo sapiens, Similar to RIKEN cDNA 1110060O18 gene, clone MGC:17236 IMAGE:3864137, mRNA, complete cds SEQ ID NO: 65 (DNA)	Consensus includes gb:AA524690 /FEA=EST /DB_XREF=gi:2265618 /DB_XREF=est:ng38e07.s1 /CLONE=IMAGE:937092 /UG=Hs.294143 ESTs, Weakly similar to predicted using Genefinder C.elegans	226168_at
hypothetical protein FLJ20209 SEQ ID NO: 66 (DNA)	Consensus includes gb:BF111925 /FEA=EST /DB_XREF=gi:10941704 /DB_XREF=est:7l38g05.x1 /CLONE=IMAGE:3523784 /UG=Hs.3685 hypothetical protein FLJ20209	226171_at
Homo sapiens mRNA for KIAA1190 protein, partial cds SEQ ID NOS: 67 (DNA) and 173 (amino acid)	Consensus includes gb:AA532640 /FEA=EST /DB_XREF=gi:2276894 /DB_XREF=est:nj17c04.s1 /CLONE=IMAGE:986598 /UG=Hs.206259 Homo sapiens mRNA for KIAA1190 protein, partial cds	226484_at
KIAA1543 protein SEQ ID NOS: 68 (DNA) and 174 (amino acid)	Consensus includes gb:AB040976.1 /DEF=Homo sapiens mRNA for KIAA1543 protein, partial cds. /FEA=mRNA /GEN=KIAA1543 /PROD=KIAA1543 protein /DB_XREF=gi:7959352 /UG=Hs.17686 KIAA1543 protein	226494_at
hypothetical protein MGC20702 SEQ ID NO: 69 (DNA)	Consensus includes gb:AK002203.1 /DEF=Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786. /FEA=mRNA /DB_XREF=gi:7023932 /UG=Hs.10260 Homo sapiens cDNA FLJ11341 fis, clone PLACE1010786	226992_at
Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	Consensus includes gb:AA129774 /FEA=EST /DB_XREF=gi:1690185 /DB_XREF=est:zl16h09.s1	227019_at

SEQ ID NO: 70 (DNA)	/CLONE=IMAGE:502145 /UG=Hs.288905 Homo sapiens cDNA FLJ13137 fis, clone NT2RP3003150	
hypothetical protein FLJ23563 SEQ ID NO: 71 (DNA)	Consensus includes gb:AW138767 /FEA=EST /DB_XREF=gi:6143085 /DB_XREF=est:UI-H-BI1-aep-a-12-0-UI.s1 /CLONE=IMAGE:2719799 /UG=Hs.274256 hypothetical protein FLJ23563	227180_at
ESTs SEQ ID NO: 72 (DNA)	Consensus includes gb:AW264333 /FEA=EST /DB_XREF=gi:6641075 /DB_XREF=est:xq98e01.x1 /CLONE=IMAGE:2758680 /UG=Hs.21835 ESTs	227320_at
ESTs SEQ ID NO: 73 (DNA)	Consensus includes gb:BF589359 /FEA=EST /DB_XREF=gi:11681683 /DB_XREF=est:nab25d01.x1 /CLONE=IMAGE:3266737 /UG=Hs.13256 ESTs	227354_at
Homo sapiens, Similar to RIKEN cDNA 1810037C20 gene, clone MGC:21481 IMAGE:3852062, mRNA, complete cds SEQ ID NO: 74 (DNA)	Consensus includes gb:AW001287 /FEA=EST /DB_XREF=gi:5848203 /DB_XREF=est:wu27e06.x1 /CLONE=IMAGE:2521282 /UG=Hs.61265 ESTs, Weakly similar to G786_HUMAN PROTEIN GS3786 H.sapiens	227676_at
ESTs, Weakly similar to JX0331 laurate omega-hydroxylase [H.sapiens] SEQ ID NO: 75 (DNA)	Consensus includes gb:AA557324 /FEA=EST /DB_XREF=gi:2327801 /DB_XREF=est:nl81a02.s1 /CLONE=IMAGE:1057034 /UG=Hs.26040 ESTs, Weakly similar to fatty acid omega-hydroxylase H.sapiens	227702_at
Homo sapiens cDNA: FLJ22063 fis, clone HEP10326 SEQ ID NO: 76 (DNA)	Consensus includes gb:T86159 /FEA=EST /DB_XREF=gi:714511 /DB_XREF=est:yd84h07.s1 /CLONE=IMAGE:114973 /UG=Hs.10450 Homo sapiens cDNA: FLJ22063 fis, clone HEP10326	227724_at
GalNAc alpha-2, 6-sialyltransferase I, long form SEQ ID NOS: 77 (DNA) and 175 (amino acid)	Consensus includes gb:Y11339.2 /DEF=Homo sapiens mRNA for GalNAc alpha-2, 6-sialyltransferase I, long form. /FEA=mRNA /PROD=GalNAc alpha-2,6-sialyltransferase I /DB_XREF=gi:7576275 /UG=Hs.105352 GalNAc alpha-2, 6-sialyltransferase I, long form	227725_at

ESTs, Weakly similar to JE0350 Anterior gradient-2 [H.sapiens] SEQ ID NO: 78 (DNA)	Consensus includes gb:AI827789 /FEA=EST /DB_XREF=gi:5448449 /DB_XREF=est:wf33a07.x1 /CLONE=IMAGE:2357364 /UG=Hs.100686 ESTs, Weakly similar to JE0350 Anterior gradient-2 H.sapiens	228241_at
ESTs SEQ ID NO: 79 (DNA)	Consensus includes gb:AI700341 /FEA=EST /DB_XREF=gi:4988241 /DB_XREF=est:wd06e10.x1 /CLONE=IMAGE:2327370 /UG=Hs.110406 ESTs	228653_at
ESTs SEQ ID NO: 80 (DNA)	Consensus includes gb:BG494007 /FEA=EST /DB_XREF=gi:13455521 /DB_XREF=est:602542289F1 /CLONE=IMAGE:4673182 /UG=Hs.203213 ESTs	228716_at
anterior gradient 2 (Xenepus laevis) homolog SEQ ID NO: 81 (DNA)	Consensus includes gb:AI922323 /FEA=EST /DB_XREF=gi:5658287 /DB_XREF=est:wn90h03.x1 /CLONE=IMAGE:2453141 /UG=Hs.293380 ESTs	228969_at
Homo sapiens cDNA: FLJ23331 fis, clone HEP12664 SEQ ID NO: 82 (DNA)	Consensus includes gb:AK026984.1 /DEF=Homo sapiens cDNA: FLJ23331 fis, clone HEP12664. /FEA=mRNA /DB_XREF=gi:10439980 /UG=Hs.50742 Homo sapiens cDNA: FLJ23331 fis, clone HEP12664	229021_at
ESTs SEQ ID NO: 83 (DNA)	Consensus includes gb:AI559300 /FEA=EST /DB_XREF=gi:4509505 /DB_XREF=est:tq43d03.x1 /CLONE=IMAGE:2211557 /UG=Hs.294140 ESTs	229331_at
hypothetical protein SEQ ID NO: 84 (DNA)	Consensus includes gb:AI830823 /FEA=EST /DB_XREF=gi:5451416 /DB_XREF=est:wj52b06.x1 /CLONE=IMAGE:2406419 /UG=Hs.95549 hypothetical protein	229439_s_at
ESTs SEQ ID NO: 85 (DNA)	Consensus includes gb:BF431989 /FEA=EST /DB_XREF=gi:11444103 /DB_XREF=est:nab84a05.x1 /CLONE=IMAGE:3274280 /UG=Hs.203213 ESTs	229657_at
ESTs SEQ ID NO: 86 (DNA)	Consensus includes gb:BF589413 /FEA=EST /DB_XREF=gi:11681737 /DB_XREF=est:nab26b11.x1 /CLONE=IMAGE:3267020 /UG=Hs.55501	229893_at

	ESTs	
brain-specific protein p25 alpha SEQ ID NO: 87 (DNA)	Consensus includes gb:BG055052 /FEA=EST /DB_XREF=gi:12512386 /DB_XREF=est:nac94g06.x1 /CLONE=IMAGE:3441995 /UG=Hs.29353 brain-specific protein p25 alpha	230104_s_at
ESTs, Weakly similar to MMHUE4 erythrocyte membrane protein 4.1, parent splice form [H.sapiens] SEQ ID NO: 88 (DNA)	Consensus includes gb:BF110588 /FEA=EST /DB_XREF=gi:10940278 /DB_XREF=est:7n39e12.x1 /CLONE=IMAGE:3567071 /UG=Hs.150478 ESTs, Weakly similar to KIAA0987 protein H.sapiens	230645_at
ESTs SEQ ID NO: 89 (DNA)	Consensus includes gb:BF592062 /FEA=EST /DB_XREF=gi:11684386 /DB_XREF=est:7n98h06.x1 /CLONE=IMAGE:3572962 /UG=Hs.233890 ESTs	230760_at
hepatocyte nuclear factor 4, alpha SEQ ID NO: 90 (DNA)	Consensus includes gb:AI032108 /FEA=EST /DB_XREF=gi:3250320 /DB_XREF=est:ow92d11.x1 /CLONE=IMAGE:1654293 /UG=Hs.54424 hepatocyte nuclear factor 4, alpha	230914_at
ESTs SEQ ID NO: 91 (DNA)	Consensus includes gb:AW203959 /FEA=EST /DB_XREF=gi:6503431 /DB_XREF=est:UI-H-BI1-aeu-b-12-0-UI.s1 /CLONE=IMAGE:2720590 /UG=Hs.149532 ESTs	230944_at
ESTs SEQ ID NO: 92 (DNA)	Consensus includes gb:AI139990 /FEA=EST /DB_XREF=gi:3647447 /DB_XREF=est:qa47d03.x1 /CLONE=IMAGE:1689893 /UG=Hs.134586 ESTs	231022_at
ESTs SEQ ID NO: 93 (DNA)	Consensus includes gb:AI806131 /FEA=EST /DB_XREF=gi:5392697 /DB_XREF=est:wf06c06.x1 /CLONE=IMAGE:2349802 /UG=Hs.99376 ESTs	231148_at
hypothetical protein FLJ23045 SEQ ID NO: 94 (DNA)	Consensus includes gb:AB046810.1 /DEF=Homo sapiens mRNA for KIAA1590 protein, partial cds. /FEA=mRNA /GEN=KIAA1590 /PROD=KIAA1590 protein /DB_XREF=gi:10047254 /UG=Hs.101774 hypothetical protein FLJ23045	232083_at
Homo sapiens cDNA:	Consensus includes gb:AK026404.1	232321_at

FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA SEQ ID NO: 95 (DNA)	/DEF=Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA. /FEA=mRNA /DB_XREF=gi:10439257 /UG=Hs.271819 Homo sapiens cDNA: FLJ22751 fis, clone KAIA0483, highly similar to AF016692 Homo sapiens small intestinal mucin (MUC3) mRNA	
Homo sapiens PAC clone RP5-855D21 SEQ ID NOS: 96 (DNA), 176 (amino acid), 177 (amino acid), and 178 (amino acid)	Consensus includes gb:AC004908 /DEF=Homo sapiens PAC clone RP5-855D21 /FEA=CDS_3 /DB_XREF=gi:4156179 /UG=Hs.249181 Homo sapiens PAC clone RP5-855D21	232641_at
putative microtubule-binding protein SEQ ID NO: 97 (DNA)	Consensus includes gb:AJ251708.1 /DEF=Homo sapiens partial mRNA for putative microtubule-binding protein. /FEA=mRNA /PROD=putative microtubule-binding protein /DB_XREF=gi:6491740 /UG=Hs.326544 putative microtubule-binding protein	234669_x_at
ESTs SEQ ID NO: 98 (DNA)	Consensus includes gb:AI741469 /FEA=EST /DB_XREF=gi:5109757 /DB_XREF=est:wg11b01.x1 /CLONE=IMAGE:2364745 /UG=Hs.57787 ESTs	234970_at
ESTs SEQ ID NO: 99 (DNA)	Consensus includes gb:AI417897 /FEA=EST /DB_XREF=gi:4261401 /DB_XREF=est:tg55b06.x1 /CLONE=IMAGE:2112659 /UG=Hs.235860 ESTs	235444_at
ESTs SEQ ID NO: 100 (DNA)	Consensus includes gb:AA827649 /FEA=EST /DB_XREF=gi:2900090 /DB_XREF=est:od01a12.s1 /CLONE=IMAGE:1357918 /UG=Hs.105317 ESTs	235515_at
ESTs SEQ ID NO: 101 (DNA)	Consensus includes gb:AI493909 /FEA=EST /DB_XREF=gi:4394912 /DB_XREF=est:qz94e02.x1 /CLONE=IMAGE:2042234 /UG=Hs.6131 ESTs	235562_at
ESTs SEQ ID NO: 102 (DNA)	Consensus includes gb:AV741130 /FEA=EST /DB_XREF=gi:10858711 /DB_XREF=est:AV741130 /CLONE=CBCATB06 /UG=Hs.173704	235651_at

	ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens	
ESTs, Weakly similar to I38588 reverse transcriptase homolog [H.sapiens] SEQ ID NO: 103 (DNA)	Consensus includes gb:AI864053 /FEA=EST /DB_XREF=gi:5528160 /DB_XREF=est:wj55h10.x1 /CLONE=IMAGE:2406787 /UG=Hs.39972 ESTs, Weakly similar to I38588 reverse transcriptase homolog H.sapiens	235678_at
ESTs SEQ ID NO: 104 (DNA)	Consensus includes gb:AW339510 /FEA=EST /DB_XREF=gi:6836136 /DB_XREF=est:xz91h08.x1 /CLONE=IMAGE:2871615 /UG=Hs.42722 ESTs	235866_at
ESTs SEQ ID NO: 105 (DNA)	Consensus includes gb:AI076192 /FEA=EST /DB_XREF=gi:3405370 /DB_XREF=est:oz01g07.x1 /CLONE=IMAGE:1674108 /UG=Hs.131933 ESTs	236422_at
ESTs SEQ ID NO: 106 (DNA)	Consensus includes gb:AL044570 /FEA=EST /DB_XREF=gi:5432785 /DB_XREF=est:DKFZp434L082_s1 /CLONE=DKFZp434L082 /UG=Hs.147975 ESTs	236548_at
ESTs SEQ ID NO: 107 (DNA)	Consensus includes gb:AI968097 /FEA=EST /DB_XREF=gi:5764915 /DB_XREF=est:wu13a12.x1 /CLONE=IMAGE:2516830 /UG=Hs.131360 ESTs	237835_at
ESTs SEQ ID NO: 108 (DNA)	Consensus includes gb:AI733801 /FEA=EST /DB_XREF=gi:5054914 /DB_XREF=est:qk39c04.x5 /CLONE=IMAGE:1871334 /UG=Hs.146186 ESTs	237923_at
ESTs SEQ ID NO: 109 (DNA)	Consensus includes gb:BF594323 /FEA=EST /DB_XREF=gi:11686647 /DB_XREF=est:7h79g07.x1 /CLONE=IMAGE:3322236 /UG=Hs.158989 ESTs	238103_at
Homo sapiens, clone MGC:16402 IMAGE:3940360, mRNA, complete cds SEQ ID NO: 110 (DNA)	Consensus includes gb:T69015 /FEA=EST /DB_XREF=gi:680163 /DB_XREF=est:yc31f04.s1 /CLONE=IMAGE:82303 /UG=Hs.192728 ESTs	238422_at

ESTs SEQ ID NO: 111 (DNA)	Consensus includes gb:AA502384 /FEA=EST /DB_XREF=gi:2237351 /DB_XREF=est:ne27f11.s1 /CLONE=IMAGE:898605 /UG=Hs.151529 ESTs	238956_at
ESTs SEQ ID NO: 112 (DNA)	Consensus includes gb:AI739241 /FEA=EST /DB_XREF=gi:5101222 /DB_XREF=est:wi14h02.x1 /CLONE=IMAGE:2390259 /UG=Hs.171480 ESTs	238984_at
ESTs SEQ ID NO: 113 (DNA)	Consensus includes gb:AA088446 /FEA=EST /DB_XREF=gi:1633958 /DB_XREF=est:zl89f04.s1 /CLONE=IMAGE:511807 /UG=Hs.170298 ESTs	239065_at
ESTs SEQ ID NO: 114 (DNA)	Consensus includes gb:AI493046 /FEA=EST /DB_XREF=gi:4394049 /DB_XREF=est:qz49b04.x1 /CLONE=IMAGE:2030191 /UG=Hs.146133 ESTs	239148_at
ESTs SEQ ID NO: 115 (DNA)	Consensus includes gb:AI243098 /FEA=EST /DB_XREF=gi:3838495 /DB_XREF=est:qh26e03.x1 /CLONE=IMAGE:1845820 /UG=Hs.178398 ESTs	239966_at
ESTs, Weakly similar to A49175 Motch B protein - mouse [M.musculus] SEQ ID NO: 116 (DNA)	Consensus includes gb:AI633523 /FEA=EST /DB_XREF=gi:4684853 /DB_XREF=est:th68b11.x1 /CLONE=IMAGE:2123805 /UG=Hs.44705 ESTs	240106_at
ESTs SEQ ID NO: 117 (DNA)	Consensus includes gb:AI300126 /FEA=EST /DB_XREF=gi:3959472 /DB_XREF=est:qn54f02.x1 /CLONE=IMAGE:1902075 /UG=Hs.257858 ESTs	240830_at
ESTs SEQ ID NO: 118 (DNA)	Consensus includes gb:AI917390 /FEA=EST /DB_XREF=gi:5637245 /DB_XREF=est:ts79a05.x1 /CLONE=IMAGE:2237456 /UG=Hs.99415 ESTs	240964_at
betacellulin SEQ ID NO: 119 (DNA)	Consensus includes gb:AI620677 /FEA=EST /DB_XREF=gi:4629803 /DB_XREF=est:tu85e09.x1 /CLONE=IMAGE:2257864 /UG=Hs.154191 ESTs	241412_at
ESTs	Consensus includes gb:H05025 /FEA=EST	241874_at

SEQ ID NO: 120 (DNA)	/DB_XREF=gi:868577 /DB_XREF=est:yl74g12.s1 /CLONE=IMAGE:43864 /UG=Hs.323767 ESTs	
ESTs SEQ ID NO: 121 (DNA)	Consensus includes gb:AW024656 /FEA=EST /DB_XREF=gi:5878186 /DB_XREF=est:wu78h05.x1 /CLONE=IMAGE:2526201 /UG=Hs.233382 ESTs, Moderately similar to AF119917 62 PRO2822 H.sapiens	242358_at
ESTs SEQ ID NO: 122 (DNA)	Consensus includes gb:BF696216 /FEA=EST /DB_XREF=gi:11981624 /DB_XREF=est:602124536F1 /CLONE=IMAGE:4281632 /UG=Hs.188724 ESTs	242626_at
ESTs SEQ ID NO: 123 (DNA)	Consensus includes gb:N57929 /FEA=EST /DB_XREF=gi:1201819 /DB_XREF=est:yv61e06.s1 /CLONE=IMAGE:247234 /UG=Hs.48100 ESTs	242978_x_at
ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY [H.sapiens] SEQ ID NO: 124 (DNA)	Consensus includes gb:AI457984 /FEA=EST /DB_XREF=gi:4312002 /DB_XREF=est:tj66a04.x1 /CLONE=IMAGE:2146446 /UG=Hs.165900 ESTs, Weakly similar to ALUC_HUMAN !!!! ALU CLASS C WARNING ENTRY !!! H.sapiens	243729_at
ESTs SEQ ID NO: 125 (DNA)	Consensus includes gb:AA581439 /FEA=EST /DB_XREF=gi:2359211 /DB_XREF=est:nh13c10.s1 /CLONE=IMAGE:952242 /UG=Hs.152328 ESTs	244650_at

Biological Validation of Biomarker Candidates: Modulation of Expression by Treatment with Ligands for EGFR or by Treatment with Inhibitors for EGFR

To validate the significance of the biomarker candidates to predict the activity of the EGFR pathway and thereby the sensitivity of cancer cell to inhibition of EGFR by therapy, genes that would be regulated by the EGFR pathway were identified. Demonstration of that property for the EGFR biomarker candidates described above would add additional credibility as it would link these genes functionally to the EGFR pathway. Colon cancer and a lung cancer cell lines were treated with epidermal

growth factor, in the absence of serum or, in the presence of serum with the EGFR modulator BMS-461453 or the EGFR modulator cetuximab (also known as C225, a chimeric monoclonal EGFR antibody). To identify genes induced by epidermal growth factor, serum starved cells were treated with 20ng/ml EGF for 0.5, 6, and 18 hours. Control cells were treated with media alone. The expression profiling was performed, and data was analyzed using GeneChip® Expression Analysis software MAS 5.0 (Affymetrix, Santa Clara, California).

Genes inhibited by EGFR antagonists were identified by treating cells in the presence of 10% serum with 0.5uM of BMS-461453 or 1ug/ml or 5ug/ml of C225 for 6 and 24 hours. Cells exposed to 0.05% DMSO were used as the experimental control. Expression profiling was performed, and data were analyzed using GeneChip® Expression Analysis software MAS 5.0.

The gene expression of the inhibitor or EGFR treated cell lines was compared pair-wise to the untreated controls. Polynucleotides from the biomarker list, in which expression was increased two fold with EGFR exposure or decreased two fold with EGFR inhibitor treatment compared to the untreated controls, were considered to be modulated by EGFR. These biomarkers are provided in Table 4. Examples of the biomarkers include EphA1, B-cell translocation gene 2, prostaglandin-endoperoxide synthase 2 and serine (or cysteine) proteinase inhibitor (clade B), which are highly expressed in sensitive cells and up regulated by treatment with EGFR. On the other hand, spondin 1, talin 2 and nuclear receptor subfamily 3 are genes whose expression levels correlate with sensitivity or resistance of colon cancer cell lines and are consistently down regulated by treatment with EGFR inhibitors BMS-461453 and C225. It appears that these biomarkers are likely to be directly or indirectly involved in the EGFR signaling pathway, based on their expression modulation by EGF or EGFR inhibitor treatment.

Identification of Top Biomarkers

In an attempt to further prioritize biomarkers for use in predicting response of cancer cells to treatment with one or more EGFR modulators, the following filter criteria were used on the Table 4 biomarkers to identify a total of fourteen biomarkers (Table 5) as the top biomarkers:

(1) results from the highly significant correlation of gene expression with IC_{50}: A p-value < 0.01 in the student TTEST or a Pearson value < – 0.6 described above;

(2) results from the modulation of expression by EGFR ligand and/or EGFR inhibitor treatment described above; and

(3) biomarkers supported by literature revealing a direct relationship between the EGFR pathway and the biomarkers.

TABLE 5 - Top Fourteen Biomarkers

Biomarker Name	Literature Support Citation	Induced by EGF/ Inhibited by EGFR antagonist
mucin 2, intestinal/tracheal (MUC2)	J Biol Chem. 2002 Aug 30;277(35):32258-67	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
intestinal mucin 3 (MUC3)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
Homo sapiens cystic fibrosis transmembrane conductance regulator ATP-binding cassette (sub-family C, member 7) (CFTR)	No	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
f-spondin (KIAA0762) protein	No	Expression inhibited 2 fold by EGFR antagonist in LOVO colon cancer cell line
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	J Invest Dermatol. 2000 Jan;114(1):83-7	Expression stimulated 3 fold by EGFR in H292 lung cancer cell line
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5	Electrophoresis. 2001 Aug;22(14):3001-8.	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
BTG family, member 2 (BTG2)	No	Expression stimulated 2 fold by EGFR in H292 lung cancer cell line
talin 2 (TLN2)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
arachidonic acid	J Biol Chem. 1994 Aug	no

epoxygenase	26;269(34):21786-92.	
prostaglandin G/H synthase and cyclooxygenase	J Biol Chem. 1994 Aug 26;269(34):21786-92.	Expression stimulated 6 fold by EGFR in H292 lung cancer cell line
EphA1 (EPHA1)	No	Expression stimulated 2 fold by EGFR in CACO2 colon cancer cell line
hemoglobin, alpha 1 (HBA1)	No	Expression inhibited 2 fold by EGFR antagonist in GEO colon cancer cell line
bone morphogenetic protein 2	Development 2000 Nov;127(22):4993-5005	no
betacellulin (BTC)*	Biochem Biophys Res Commun. 2002 Jun 28;294(5):1040-6	no

*The gene betacellulin showed counter regulation with EGFR expression as defined for the EGFR-A list but had just a p value of 0.04 in the Student's TTest for correlation with IC_{50}. It was still selected as a top biomarker for the strong literature support, as betacellulin is one of the published ligands of EGFR.

Utility of Biomarkers

Polynucleotides that correlate to a specific property of a biological system can be used to make predictions about that biological system and other biological systems. To show the predictive utility of biomarkers that correlate to EGFR modulator sensitivity and resistance, these polynucleotides were tested for their ability to predict the response of twenty two colon cancer cell lines to a small molecule EGFR modulator.

The invention includes single biomarkers including, for example, the fourteen top biomarkers which were tested in a voting scheme. For that purpose, the mean expression value was calculated for all fourteen biomarkers. Colon cancer cell lines which showed an expression level above the mean were then voted to be sensitive, and colon cancer cell lines with expression levels below the mean were voted to be resistant. After this procedure, the voting was compared to the actual sensitivity/resistance status according to the definition based on IC_{50} (see above) and an error rate was calculated. The error rates of the fourteen top biomarkers are shown in Table 6.

TABLE 6 - Error Rates of Fourteen Top Biomarkers

Biomarker Name	Pearsons value	TTEST P value	Prediction error rate
mucin 2,	-0.531	0.0083	20%

intestinal/tracheal (MUC2)			
intestinal mucin 3 (MUC3)	-0.639	0.0004	11.72%
Homo sapiens cystic fibrosis transmembrane conductance regulator ATP-binding cassette (sub-family C, member 7) (CFTR)	-0.646	9E-05	5.9%
f-spondin (KIAA0762) protein	-0.622	0.0004	12.8%
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-0.575	0.0029	21.75%
serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5 (SERPINB5	-0.62	0.0028	21.75%
BTG family, member 2 (BTG2)	-0.544	0.0042	20.5%
talin 2 (TLN2)	-0.874	3E-05	8.8%
EphA1 (EPHA1)	-0.647	0.0021	22%
hemoglobin, alpha 1 (HBA1)	-0.744	8E-05	20%
bone morphogenetic protein 2	-0.555	0.0091	31.8%
betacellulin (BTC)	-0.536	0.047	43.5%

The biomarkers talin, the Cystic fibrosis conductance regulator (CFTR), and mucin 3 were the best single biomarkers with error rates below 12%.

EXAMPLES:

EXAMPLE 1 - METHODS

IC50 determination--*in vitro* cytotoxicity assay

A small molecule EGFR inhibitor, erlotinib HCl (BMS-461453), was tested for cytoxicity *in vitro* against a panel of twenty-two human colon cancer cell lines

available from the American Type Culture Collection. Cytotoxicity was assessed in cells by MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphenyl)-2H-tetrazolium, inner salt) assay (T.L. Riss et al., 1992, *Mol. Biol. Cell*, 3 (Suppl.):184a).

To carry out the assays, the colon cells were plated at 4,000 cell/well in 96 well microtiter plates and 24 hours later serial diluted drugs were added. The concentration range for the EGFR inhibitor was from 5 μg/ml to 0.0016 μg/ml (roughly 10 μM to 0.0032 μM). The cells were incubated at 37 °C for 72 hours at which time the tetrazolium dye MTS (333 μg/ml final concentration) in combination with the electron coupling agent phenazine methosulfate (25 μM final concentration) was added. A dehydrogenase enzyme in live cells reduces the MTS to a form that absorbs light at 492 nm that can be quantified spectrophotometrically. The greater the absorbency, the greater the number of live cells. The results were expressed as an IC_{50}, which is the drug concentration required to inhibit cell proliferation (i.e., absorbance at 450 nm) to 50% of that of untreated control cells. The mean IC_{50} and standard deviation (SD) from multiple tests for each cell line were calculated.

Resistant/sensitive classification

The cell lines with IC_{50} below 6 μM were defined as sensitive to the EGFR inhibitor, whereas those with IC_{50} above 6 μM were considered to be resistant. The resistant/sensitive classification are shown above in Table 1, with five cell lines classified as sensitive and seventeen cell lines classified as resistant.

Gene expression profiling

The colon cells were grown using standard cell culture conditions: RPMI 1640 supplemented to contain 10% fetal bovine serum, 100 IU/ml penicillin, 100 mg/ml streptomycin, 2 mM L-glutamine and 10 mM Hepes (all from GibcoBRL, Rockville, Maryland). RNA was isolated from 50-70% confluent cells or drug-treated cells using the RNeasy™ kits commercially available from Qiagen (Valencia, California). Quality of the RNA was checked by measuring the 28s:18s ribosomal RNA ratio using Agilent 2100 bioanalyzer (Agilent, Technologies, Rockville, Maryland). Concentration of total RNA was determined spectrophotometrically. 10

μg of total RNA from each cell line was used to prepare biotinylated probe according to the Affymetrix Genechip® Expression Analysis Technical Manual, 2001. Targets were hybridized to Affymetrix high density oligonucleotide array human HG-U133 set chips (Affymetrix, Santa Clara, California). Arrays were then washed, and stained using the GeneChip Fluidics station according to the manufacture's instructions. The HG-U133 set consisting of two GeneChip® arrays contains nearly 45,000 probe sets representing more than 39,000 transcripts derived from approximately 33,000 well-substantiated human genes.

Preprocessing of microarray data for selecting biomarkers

Scanned image files were visually inspected for artifacts and analyzed with GeneChip® Expression Analysis software MAS 5.0 (Affymetrix, Santa Clara, California). The "Detection Call" (see Affymetrix manual) was used to determine whether a transcript was detected within one sample, as well as the "Signal" (see Affymetrix Genechip® Expression Analysis Technical Manual, 2001) which measured the relative abundance of a transcript. The trimmed mean intensity for each chip was scaled to 1,500 (see Affymetrix manual) in order to account for any minor differences in global chip intensity, so that the overall expression level for each cell line is comparable. Affymetrix control sequences were removed prior to analysis.

Induction Studies of colon and breast cell lines with EGFR inhibitors or EGFR ligand and selection of genes modulated by the inductions

The five colon cell lines and one lung cell line indicated with asterisks in Table 1 were used in the drug induction study. Three of the colon cell lines express EGFR and are sensitive to the EGFR inhibitor BMS-461453. The SW480 cell line, while expressing EGFR, is insensitive to the EGFR inhibitor, and the COLO320_DM does not express EGFR and is EGFR inhibitor resistant. The lung cancer cell line H292 expresses EGFR, but its sensitivity status is unknown. Cells were seeded in a 10 cm^2 culture plate with the medium described above and cultured for 24 hours.

For the EGF induction studies, the colon cell line CACO2 and the lung cancer H292 cell line were washed 2X PBS, and the media was changed to RPMI without serum. The next day the cells were treated with 20 ng/ml EGF, and eventually lysed

for RNA isolation 0.5, 6 and 18 hours post treatment. Gene expression was profiled as described below.

EGFR inhibition studies were conducted on the colon cell lines GEO, CCD33-CO, SW480 and COLO320DM. The expression profiling was performed as described above and data was analyzed using GeneChip® Expression Analysis software MAS 5.0. The expression data of EGFR inhibitor treated cell lines were compared pair-wise to that of untreated same cell line. A change was considered significant if a two fold difference in expression was demonstrated between the treated and the untreated control. Analysis was done for all four cell lines to compare the gene expression with or without EGFR inhibitor treatment.

EXAMPLE 2 - RT-PCR EXPRESSION PROFILING

RNA quantification was performed using the SYBR Green real-time PCR. The SYBR Green real-time PCR assay is one of the most precise methods for assaying the concentration of nucleic acid templates.

RNA can be prepared using standard methods, preferably, employing the RNeasy Kit commercially available from Qiagen (Valencia, California). cDNA template for real-time PCR can be generated using the Superscript™ First Strand Synthesis system for RT-PCR. SYBR Green real-time PCR reactions are prepared as follows: the reaction mix contains 20 ng first strand cDNA; 50 nM Forward Primer; 50 nM Reverse Primer; 0.75X SYBR Green I (Sigma); 1X SYBR Green PCR Buffer (50mMTris-HCl pH 8.3, 75 mM KCl); 10% DMSO; 3 mM $MgCl_2$; 300 μM each dATP, dGTP, dTTP, dCTP; 1 U Platinum® Taq DNA Polymerase High Fidelity (Cat# 11304-029; Life Technologies; Rockville, Maryland). Real-time PCR is performed using an Applied Biosystems 5700 Sequence Detection System. Conditions are 95 °C for 10 minutes (denaturation and activation of Platinum® Taq DNA Polymerase), 40 cycles of PCR (95 °C for 15 seconds, 60 °C for 1 minute). PCR products are analyzed for uniform melting using an analysis algorithm built into the 5700 Sequence Detection System.

cDNA quantification used in the normalization of template quantity is performed using SYBR Green real-time PCR. Expression of EGFR is normalized to GAPDH expression as described below.

The sequences for the GAPDH oligonucleotides used in the SYBR Green real-time PCR reactions are:

GAPDH-F: 5'-AGCCGAGCCACATCGCT-3' (SEQ ID NO: 191)

GAPDH-R: 5'-GTGACCAGGCGCCCAATAC-3' (SEQ ID NO: 192)

The sequences for the EGFR oligonucleotides used in the SYBR Green real-time PCR reactions are:

EGFR-F: 5'- GCGTCTCTTGCCGGAATGT-3' (SEQ ID NO: 193)

EGFR-R: 5'- AGCCGAGGCAGGGAATGCGTG-3' (SEQ ID NO: 194)

The Sequence Detection System generates a Ct (threshold cycle) value that is used to calculate a concentration for each input cDNA template. cDNA levels for each gene of interest are normalized to GAPDH cDNA levels to compensate for variations in total cDNA quantity in the input sample. This is done by generating GAPDH Ct values for each cell line. Ct values for the gene of interest and GAPDH are inserted into a modified version of the δδCt equation (Applied Biosystems Prism® 5700 Sequence Detection System User Manual) which is used to calculate a GAPDH normalized relative cDNA level for each specific cDNA. The δδCt equation is: relative quantity of nucleic acid template $=2^{\delta\delta Ct} = 2^{(\delta Cta-\delta Ctb)}$, where δCta = Ct target – Ct GAPDH, and δCtb = Ct reference – Ct GAPDH.

EXAMPLE 3 - PRODUCTION OF ANTIBODIES AGAINST THE BIOMARKERS

Antibodies against the biomarkers can be prepared by a variety of methods. For example, cells expressing an biomarker polypeptide can be administered to an animal to induce the production of sera containing polyclonal antibodies directed to the expressed polypeptides. In one aspect, the biomarker protein is prepared and isolated or otherwise purified to render it substantially free of natural contaminants, using techniques commonly practiced in the art. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity for the expressed and isolated polypeptide.

In one aspect, the antibodies of the invention are monoclonal antibodies (or protein binding fragments thereof). Cells expressing the biomarker polypeptide can be cultured in any suitable tissue culture medium, however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented to contain 10% fetal bovine

serum (inactivated at about 56 °C), and supplemented to contain about 10 g/l nonessential amino acids, about 1,00 U/ml penicillin, and about 100 μg/ml streptomycin.

The splenocytes of immunized (and boosted) mice can be extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line can be employed in accordance with the invention, however, it is preferable to employ the parent myeloma cell line (SP2/0), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (1981, *Gastroenterology*, 80:225-232). The hybridoma cells obtained through such a selection are then assayed to identify those cell clones that secrete antibodies capable of binding to the polypeptide immunogen, or a portion thereof.

Alternatively, additional antibodies capable of binding to the biomarker polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens and, therefore, it is possible to obtain an antibody that binds to a second antibody. In accordance with this method, protein specific antibodies can be used to immunize an animal, preferably a mouse. The splenocytes of such an immunized animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones that produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce the formation of further protein-specific antibodies.

EXAMPLE 4 - IMMUNOFLUORESCENCE ASSAYS

The following immunofluorescence protocol may be used, for example, to verify EGFR biomarker protein expression on cells or, for example, to check for the presence of one or more antibodies that bind EGFR biomarkers expressed on the surface of cells. Briefly, Lab-Tek II chamber slides are coated overnight at 4 °C with 10 micrograms/milliliter (μg/ml) of bovine collagen Type II in DPBS containing calcium and magnesium (DPBS++). The slides are then washed twice with cold DPBS++ and seeded with 8000 CHO-CCR5 or CHO pC4 transfected cells in a total

volume of 125 μl and incubated at 37 °C in the presence of 95% oxygen / 5% carbon dioxide.

The culture medium is gently removed by aspiration and the adherent cells are washed twice with DPBS++ at ambient temperature. The slides are blocked with DPBS++ containing 0.2% BSA (blocker) at 0-4 °C for one hour. The blocking solution is gently removed by aspiration, and 125 μl of antibody containing solution (an antibody containing solution may be, for example, a hybridoma culture supernatant which is usually used undiluted, or serum/plasma which is usually diluted, e.g., a dilution of about 1/100 dilution). The slides are incubated for 1 hour at 0-4 °C. Antibody solutions are then gently removed by aspiration and the cells are washed five times with 400 μl of ice cold blocking solution. Next, 125 μl of 1 μg/ml rhodamine labeled secondary antibody (e.g., anti-human IgG) in blocker solution is added to the cells. Again, cells are incubated for 1 hour at 0-4 °C.

The secondary antibody solution is then gently removed by aspiration and the cells are washed three times with 400 μl of ice cold blocking solution, and five times with cold DPBS++. The cells are then fixed with 125 μl of 3.7% formaldehyde in DPBS++ for 15 minutes at ambient temperature. Thereafter, the cells are washed five times with 400 μl of DPBS++ at ambient temperature. Finally, the cells are mounted in 50% aqueous glycerol and viewed in a fluorescence microscope using rhodamine filters.

CLAIMS:

What is claimed is:

1. A method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises:

(a) measuring in the mammal the level of at least one biomarker selected from the biomarkers of Table 4;

(b) exposing the mammal to the EGFR modulator;

(c) following the exposing of step (b), measuring in the mammal the level of the at least one biomarker,

wherein a difference in the level of the at least one biomarker measured in step (c) compared to the level of the at least one biomarker measured in step (a) indicates that the mammal will respond therapeutically to said method of treating cancer.

2. The method of claim 1 wherein the at least one biomarker is selected from the biomarkers of Table 5.

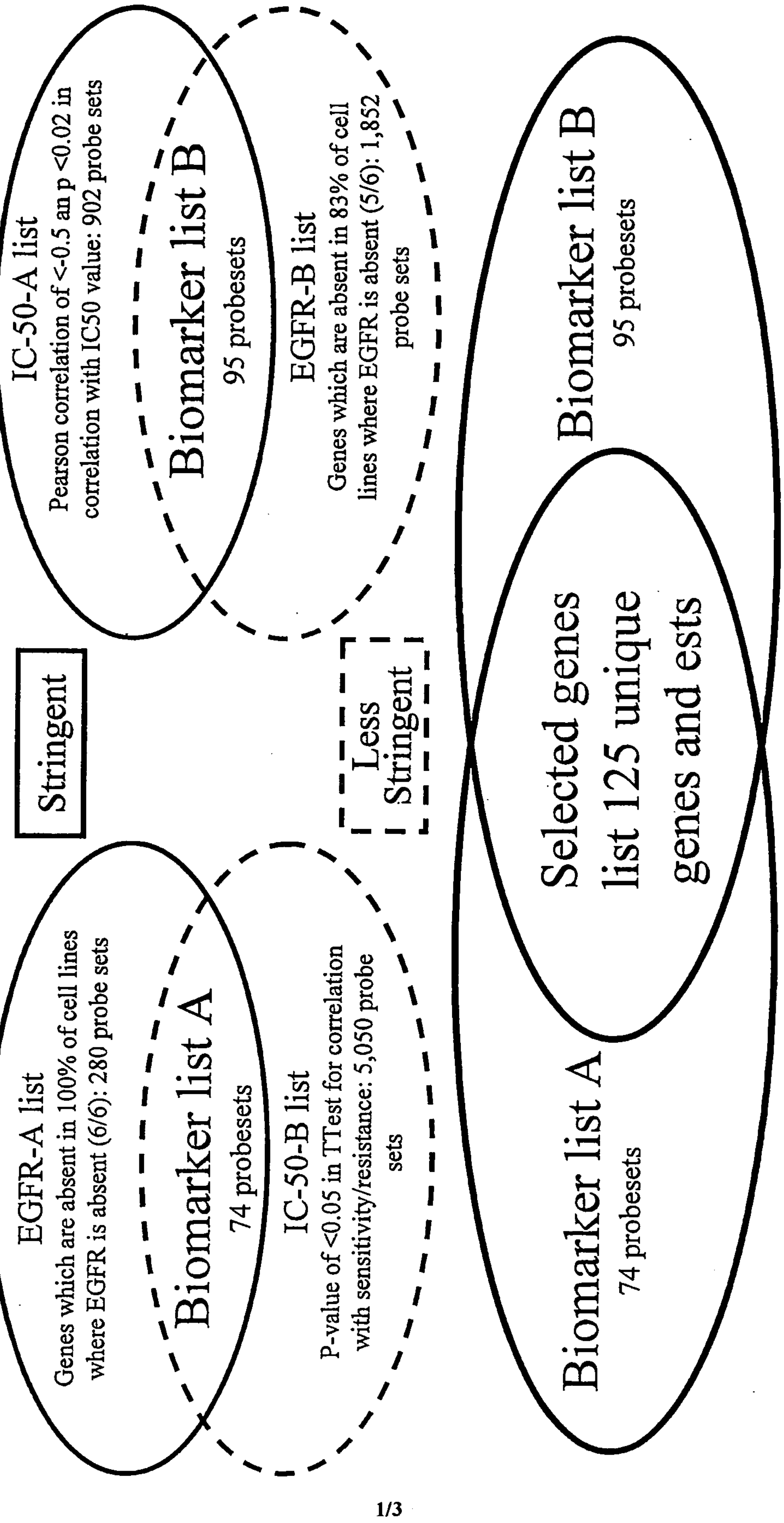
3. The method of claim 1 wherein the method is an in vitro method, and wherein the at least one biomarker is measured in at least one mammalian biological sample from the mammal.

4. A method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises:

(a) exposing the mammal to the EGFR modulator;

(b) following the exposing of step (a), measuring in the mammal the level of the at least one biomarker selected from the biomarkers of Table 4,

wherein a difference in the level of the at least one biomarker measured in step (b), compared to the level of the biomarker in a mammal that has not been exposed to said EGFR modulator, indicates that the mammal will respond therapeutically to said method of treating cancer.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EGFR-B list
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Stringent
Less Stringent
EGFR-A list
Genes which are absent in 100% of cell lines where EGFR is absent (6/6): 280 probe sets
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FIG. 1

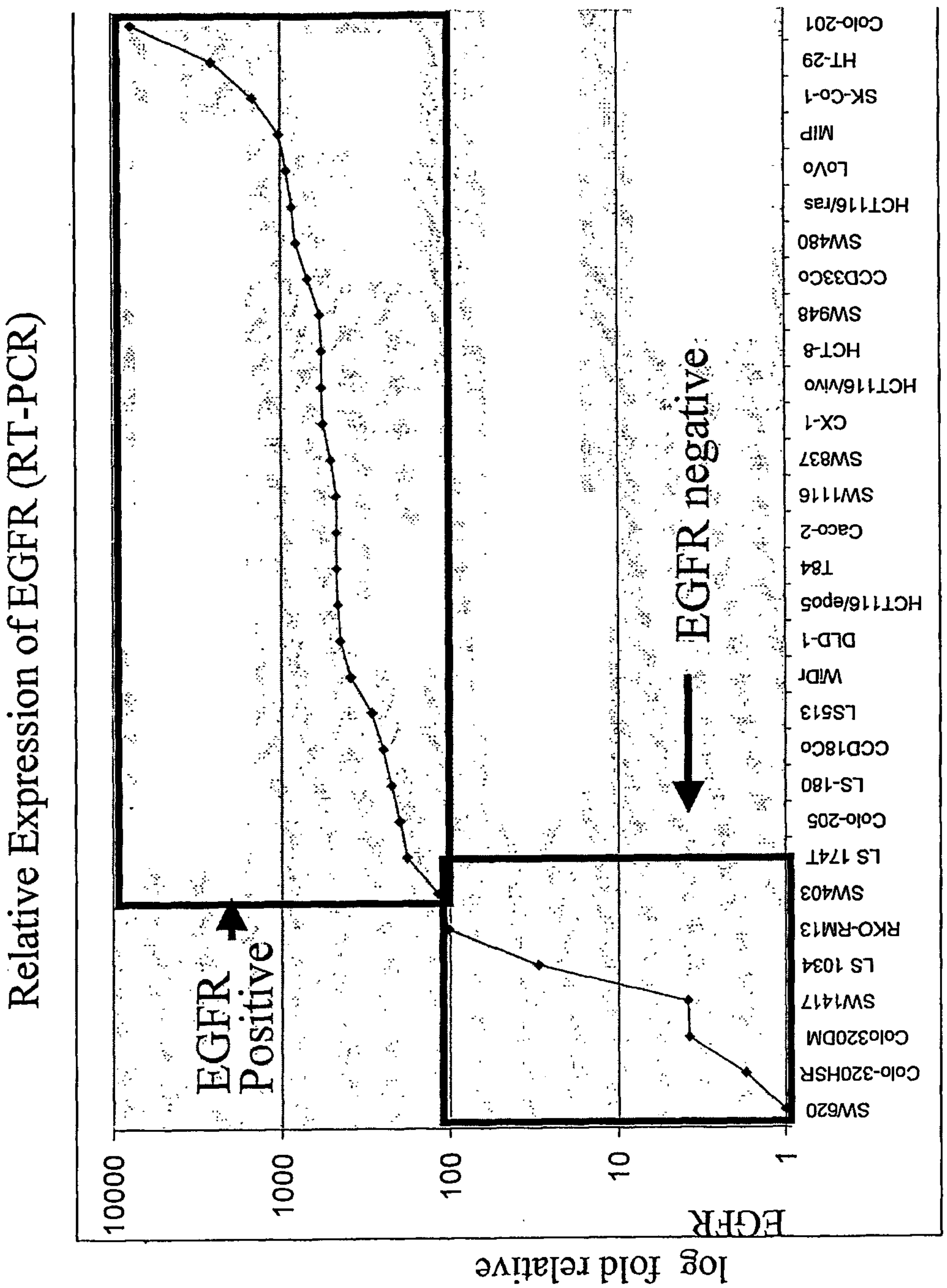
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FIG. 2A

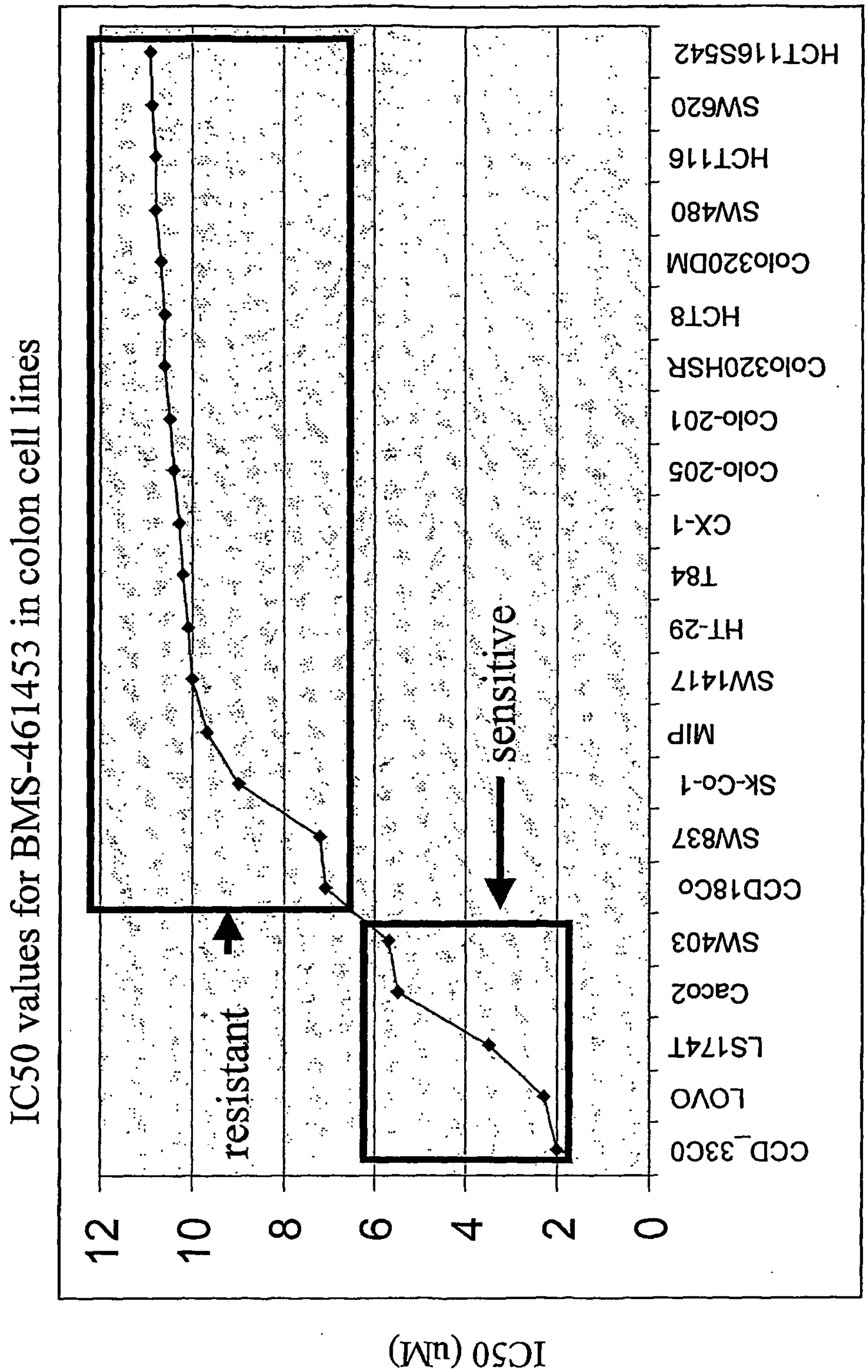
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FIG. 2B

SEQUENCE LISTING

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<213> Human

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<210> 69
<211> 1634
<212> DNA
<213> Human

<400> 69
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taactcctcc acataagcgg caggaaaatg gcctttttc ccattcaaag atccaaacca 180

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tttcaaattg ttctcatcca ttaacgctgc tgtgtctttc tggctctttg catcagagaa 600

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gcttttgtcc tttc 1634

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<211> 774
<212> DNA
<213> Human

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<223> n is a, c, g, or t

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<222> (509)..(509)
<223> n is a, c, g, or t

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<221> misc_feature
<222> (617)..(617)
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<223> n is a, c, g, or t

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<222> (693)..(693)
<223> n is a, c, g, or t

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<222> (740)..(740)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (762)..(762)
<223> n is a, c, g, or t

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ctggagccaa tcttcttctt taaacgctga tggattgcat acatgtatgt cttccatatc 180

agccacatac acaacattca gatacacttc cctctgtgca gggggataca ccagcctcct 240

gccaggttct ggaagctcac cttataatct accaggataa agctgtgtgc tgagtaggag 300

gttatggtgg ggttggggag taacaaggag ataaaagacc ttgtggtccc aacttcctta 360

tgtggacaga gaagataggt cctttactcc tcctcattac cctgccctct catggactgg 420

gctaactgaa ggccaagctc ccagagaagc tggactcact gtgtnggatt actgagggtg 480

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ttaagancca gacaccagtc ttcagagagc ctnccgaggt agccgcaaca ttcctgcagc 720

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<210> 71
<211> 578
<212> DNA
<213> Human

<400> 71
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agggtaatgg aaagaatata atctcgtaat tttatactta aggctgtaaa tggcaaagtc 180

ccatagatat ttaaaaatct atatttgtat ttatttataa tatagatata ggccctcaag 240

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tgttttatta catgttagct tataggcaag ttaaacat 578

<210> 72
<211> 475
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (285)..(285)

<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (361)..(361)
<223> n is a, c, g, or t

<400> 72
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gccccaggga accttcccct ccccttttat gcattaccag gggagtggca ggggcagccc 240

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gtctttgtct ggctcatgtt cctctcacaa catcccacag gcaggggtga gcctg 475

<210> 73
<211> 512
<212> DNA
<213> Human

<400> 73
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taattacaac atacctgcta tttacatgta atcatacttt tatatatagc ttgaataagt 120

tttattacat gtaaactata agatattaca agttaaactc cagtcttttc tggatattca 180

attgaaatac tactggcaga aacatacaga aaacaaatac ccatttcagt tcctcaggta 240

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aattggatca ttaaaaacac atcttcaatt tatatagcac ctttcttccg aagagttgaa 420

agcattcgtg cttatctcta ttatttcgtt tgtccccata acatctctat gaggtaggca 480

atggttagta tcattatccc cattttgtat at 512

<210> 74
<211> 668
<212> DNA
<213> Human

<400> 74
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tccaaaagga ccctctgagg ctggtcttcc gggtaggatg tgctgtggga gggttctgtt 180

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tgctggcg 668

<210> 75
<211> 568
<212> DNA
<213> Human

<400> 75
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<210> 76
<211> 491
<212> DNA
<213> Human

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<222> (371)..(371)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (394)..(394)
<223> n is a, c, g, or t

<400> 76
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acttatccaa t 491

<210> 77
<211> 2437
<212> DNA
<213> Human

<400> 77
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<210> 78
<211> 582
<212> DNA

<213> Human

<400> 78
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aaccattaat ggcttcttac ttttttgagc ataaaagaga ccttgctcat aagtttgtac 540

ccaagagatg gcatctaccc atcctcttga gagtgactga gg 582

<210> 79
<211> 511
<212> DNA
<213> Human

<400> 79
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acgtccttta aaaaaaataa taactgaaag ggaaaagaaa gtgtcaattg caattacatt 180

tacaaaacca aactgctgct ttcaattaga gtgaatctgt gcttcgctac tcagatatac 240

acatgtagat tttccaaggc ccatgcacac acttctgtag ggcagaaat tttctatgaa 300

taatggcttt agcaacccga atagtatctc taaacattga caagcttggg gaacagggca 360

acaagtgcaa tgaacaatac aatttctaac gtttgtccca gtcaacatac cactttgccc 420

tggagatatt taacacagca tttcattttt ggaatgataa gggataattc atctaattaa 480

gggtattata cagaatatac ctataaaaga c 511

<210> 80
<211> 987
<212> DNA
<213> Human

<400> 80
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ttgatagtga tagactataa tccatattta aattttatag agaagaaatt ttattgtact 180

gtgatgtaga tatttattat ccaggtaagg atttgcccgg tgtgtatttt ttacaattga 240

gacattttac tttaatcttt aacaaaaaat gcattaaaaa cacactcaaa aaaaaacaaa 300

aaaaaaaaaa aaagacaacc caaacggggg gggaaaaaag aggtgattgg cacccttttat 360

cacgaaaatc ttcctgcggg cggccctcta ataaccagtc ttctggaaca actgtgccca 420

aaccgaggtg tcgctcttta aaataggcgt ggtctcccac catatctaac actcaaatgg 480

cgccgcctct tctcaaaaga acccacaaat atgtgtgccg accaagagtt aaaaaacccg 540

ccttgcgttg gacggggcgg acattatctt ggattggcac caacactatt aaaagaggcg 600

atgcgacacc caaccccgat taattggcag cagacagaaa tcctttctca actagtatag 660

aaaactgttg tggccctcca ccacacaaaa ggacgaatcc tacccaacta atgtattagc 720

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acacaaacac cagggaggga agacacacgc attttgtaac acaaatagat ctaatattag 840

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tgtcccgcca ctgctgctgt tcgtcggcat gttatcatgc cccacgctct ctgtgatcct 960

acacgagagg gatcacccca cgcttat 987

<210> 81
<211> 483
<212> DNA
<213> Human

<400> 81
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gaattccata tattaatgaa tgtgagatta agtatagagt gaagacatta acacacaatt 180

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acaaatcgat tacaaggtca attcccagga tttcttcagg gtgtgttcag gagtgcagat 420

gttctttgga tgacctttct actaaattag acctctgaag gagaaagcta cttgccagag 480

gct 483

<210> 82
<211> 552
<212> DNA

<213> Human

<400> 82
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cacaaaataa gctcttaatg caagaaatga atctccagga tagatcatac taatctatcc 180

aatccagccc tctgttctga aagcagcaca tgaaaaggca gagaaagaaa aataatctct 240

acgacctggc ctgttaaaca tgtatttatt tcctgagtaa ctattaggtg ctagctgtaa 300

tgggctattc agtggaggac agtggtcaaa gcctcttatg atgtatggca gatgccagaa 360

agatatgaaa gatgtgatgg tacaaaaaag gaagttggag tcacatccag ccacaggact 420

aactaagcct ctttggggca ggagactttg gaagtgttga aggagagtag aatctattca 480

gaaagaaaca actgggggca ggtccttcca gtctgaatga agattaacta ggcgtaatgt 540

aactggcatc at 552

<210> 83
<211> 505
<212> DNA
<213> Human

<400> 83
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tgttattatt agatgttaag ccgaaaatct agaaactaac atttacccag gttacaaaat 120

aagagcttca tatttttcaa agtctctaag ggtaaggtac atccccagat aaaatgagta 180

taggccagtc tcctttggct ttgtggattc tttccaaaaa ttttccagac tatttagctt 240

tccttgtgta gttacagctc aaattagaaa ctgaagaaac agcaagtggc caggcagggt 300

agaaagcaaa taaactgagc tacctgtgcc tttttccaaa tcagtatatg tgcttggctc 360

ctgaaaaaaa aaattctgat atgtaggcat tctcattact tagtgagata ttagtgaaga 420

cctttcaacg tataacacac agtaactgtt gcatagtttt aataaacact tgaattttcc 480

aggaatgtga ctgctgtgta aatca 505

<210> 84
<211> 671
<212> DNA
<213> Human

<400> 84
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atcatgtgct ccactgtgtg gattttgcca tcttcaatca ttttaggggc tggagctgct 120

ggaaacatgg aatactgagc cccaatggca gggatggcta ctgtaccagg tttaatggca 180

actgggttga cggtagggat ttccaaattc ggcaccagtt catatccttt ttcttgctgc 240

tttcctttcc cttcatgata tcggctatat ataccacggc cagcagaata tcccccgagg 300

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ctgcctgctt tcacaaagta gtccctgttg ggcccaatga gcgcgttgta ggggtagccg 420

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ttggccagcg tgacctccag gcacgagccc tccagctcag tgccggttga gttgttcatg 600

gcatgcacgg catcctcgcg gctggtgaag tgcacggagg cgtaggtccg gatcttcttg 660

acgcgctcca c 671

<210> 85
<211> 563
<212> DNA
<213> Human

<400> 85
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ctacgcccac tatattcata attacagttt tatatctgca tacaaaagct atgtaaaaat 120

ccatttttcc caaatataca aatttttttt ggatagttta aaacattttg atcacagatt 180

tcaacagagt tttaggctga aaaaaatatc accatctagc aatatcactt aacactgttt 240

gcaaaacaca aatcttccaa tgactgtaaa tctttttcta ttctgtagta tttttctgat 300

tctcagggca tgaaaacatt atgggaaaaa aaaggatttt ctacgaagaa agcatggaga 360

actaatttgg ctctatggtc aaattaaaaa tgccaagtta ataagggaga accaaaagaa 420

agaagtggca taatgtcaca tcagctcatt catgccctga taatttctgt atcaacaata 480

catatgtaaa gtgtctcctt ttgtcttaca ttgtgctcca taatttacat gagtattatc 540

tgcatcctga ggaggacaga ttt 563

<210> 86
<211> 545
<212> DNA
<213> Human

<400> 86
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agtatttcaa tgaaataaac ttattgggga ttcaccccga gttgtgttta taaatattag 180

acaaaccaca aaatatattc caaatacata acattttaca atatttttca agcacagaca 240

aatacatact ttactttacc tacattgttt tcatgatcca acttgcatta gcactaaagg 300

caatattgtg tgtgtatatg tatttgccat atgtgtgtgt gtattatata tatttattta 360

tatccacaaa tgtacactca gtggcattta tggaaaattt aacccttca ggctgtgggt 420

tttacccacc atagtatctg agagggagaa gaaccaataa tacatctcaa attcctcaat 480

tagggcaaaa taagcacaat tatgcatgag gggcatatat gttgtgtcta ttcaaagaca 540

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<210> 87
<211> 464
<212> DNA
<213> Human

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<223> n is a, c, g, or t

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<221> misc_feature
<222> (276)..(276)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (422)..(422)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (463)..(463)
<223> n is a, c, g, or t

<400> 87
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taagagaaac ttgaaaggga tcgtgtaact actagtttgt actaagtttt tttcaagaaa 180

gggaaacaaa tttatatata tatatatata tatatatatg tgcaatatat ttttacactg 240

tgtgattaac attagggagt actgagtgca tcactntatc agtgtgacgg gtgatgtcca 300

cgtcatggct gttctgactc tgaaagccac ttctgctgat gtctaaaccg cactcaccgc 360

ggacgtccgg ggttgtggtg gccctgctgt gcctcctgca ggtgagaggt gtggtgttgc 420

cngttggact tgctgttgag cctggttgca aacctgtagt gana 464

<210> 88
<211> 611
<212> DNA
<213> Human

<400> 88
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ggattatatt caacaacttt ctcttgagtt gttactaaaa ttctgattct gaaccttata 180

gcttataatg gtgccaacta ttagaaatgg gaaaatctaa ttcagtccaa tgtaacatgt 240

attatgatat aatagatgaa gggtatgtct acactataat aaaaaataaa catatttttg 300

gttatttaaa gaccatcttc ctaacctgta actaaaataa ctgtatttga tttaaactta 360

tttaagtgca gtgaattatg gaaagctaac ttaaaggttt gaataatcaa ttatgagtaa 420

ggaacacctg ttgacagccc cgtgaccctt cagaaccagg catttgctga aaaaaagaaa 480

tcactagcat tgaatatagc ccttagtcac gtgagagatt aacttcatga gcaacccagc 540

atgtagagga tgaggtggac tttcccagcc acccactcct tgaggggaca gtagtattca 600

tagtgaaact g 611

<210> 89
<211> 515
<212> DNA
<213> Human

<400> 89
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cacacttcct atatgaattc ttcatagtta ttttaagtat tttacaattt gtacagagga 120

agggacatac aatatctaat aggctatttt tcaaccaaat aataatttat gtccttgtaa 180

gattttgtac ctctttaaaa ctttcaactt caacatccac ttttttagct ttgctaatca 240

aattaagaat taaaaccagc ctgcaaataa taacagtata taacattaag cacaatttca 300

tttctttctt tatacaaatg ttctatattt acttgaccaa atgcttaatt accttttaaa 360

ggtttcaata ccgtggttaa aaacaaaaca actgtgtata cctccagact atatgaaaaa 420

tatgaaatat gtaaagtgtc acgtttttta ccttagttta tttttaaaag ataaatagct 480

aactatctgt attaatttta aagaatgttt taaaa 515

<210> 90
<211> 535
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (422)..(422)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (424)..(424)
<223> n is a, c, g, or t

<400> 90
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gcctcaggcc aatcttggtc ctgggagtgg gcagggttcc cagaagaacg agtctggttt 120

ctgaggctgt agaagggagc cggaagcccc tcaacttgat cacggtgaga acacagggag 180

cctttggaga agctattcag ccactgtagt taagagctcc tgttctgatc cagggagacc 240

tgggttcaag tcctgactca gccacttcct agttgtgtga gtttcagaaa aaaaatcact 300

tcacctctta gaacgcaatt tcagcttctg taacaatctc taggttagga gggagtgggg 360

cgggtgaggg cggggagggg agaggaaaaa aaaacacaac aatctctatg tggtttaagg 420

gnanggggggt taaatgagat gatcatgaca atgcctatag aagtgctggg agtatgaaag 480

ctggaacagc cctgtgagct ttgtgtcgtt gtccgatttt tgataagggc aaata 535

<210> 91
<211> 535
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (97)..(97)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (322)..(322)
<223> n is a, c, g, or t

<400> 91
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gtaaatggct tcccaaggtc acagtggtgt cagtggcaga gctggtactg taccaggctg 180

cctggatcat agactgatgt ttttgccaag accagccgaa atgttcctct caggaggtgg 240

caggtggggg tggagtgcca ggaaggcact gtccaaagaa gtgggttaag gtcacagcct 300

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cagaggcttg aggttttgga gtggaaaggg gcagggtaag gaagaataga gtaggaggag 420

ggcgggggac agggattcat cctccaggtt cctcacaccc ccactgggag cagcgccccc 480

accccaagca cctgatttca aagtctcccc tccactgaag ggaggggcaa aggga 535

<210> 92
<211> 548
<212> DNA
<213> Human

<400> 92
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aaaataggac aacacatgta ggcaatacca agcagttctt gtggcagcaa ctggaaacct 180

tttggagaca ccattctgca tttcgttgta gtcatacaca aaaccctagt tatgtatcca 240

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aactacccaa attattgagg tgtttttgct cacttcttcc cattagaata aatgtagaca 360

ataagaaacg catgagggat gacatagtcc tccatcaaat ctgtcctttc acacaagaga 420

tggcatggtg tagtgtagca gaatcatgag ctgccaggaa attatgaatt ctgattcctc 480

cagctgagtc tttgaaaaag tccagatgag aaacacttcc atcctgatgc tgaagcaagg 540

agaatgtc 548

<210> 93
<211> 481
<212> DNA
<213> Human

<400> 93
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gcttctctac tggtacacat attaccctag cctatgtttc tgagatgcct tagtgaaagt 180

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tgtgaggcca aaggaatcaa gacagcagag ctcaaagcag ggccagaagg tgcagggggg 360

accacattgg cgggtctcgc tcagggacac gatggcgtca ttgtaacagc actgctccaa 420

ggggttgtag atcttgtctc cacacctggg tgccggctgg cacagccatg gttctgagcc 480

a 481

<210> 94
<211> 4021
<212> DNA
<213> Human

<400> 94
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ttatggtgac gtagaagaac ttatggatgc gggcaatatc aaccggacca ccgcagcgac 180

tgggatgaac gacgtcagta gcaggtctca tgccatcttc accatcaagt tcactcaggc 240

taaatttgat tctgaaatgc catgtgaaac cgtcagtaag atccacttgg ttgatcttgc 300

cggaagtgag cgtgcagatg ccaccggagc caccggggtt aggctaaagg aagggggaaa 360

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t 4021

<210> 95
<211> 2917
<212> DNA
<213> Human

<400> 95
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<211> 140
<212> DNA
<213> Human

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<222> (20)..(20)
<223> n is a, c, g, or t

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<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (72)..(72)
<223> n is a, c, g, or t

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ganatactgg anaaggctgg gccacttgtt gctgtgtctg ctgttgcact tgatataact 120

gcctacccct aaaagccaaa 140

<210> 98

<211> 492
<212> DNA
<213> Human

<400> 98
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tcacattttt tatagattaa aaaacttaaa aataaaaaag tactaagtta aaaaaaactc 120

cactaggaga ttactaaaac tgtaggccac attcatcttc ctacaattct tcacccacaa 180

aataaaatcc aatttaggag gctccattaa ctcttttaat atatttctaa atcttaaatc 240

tatatttcaa aatgaacatg gtacttcata tgggcccact tttcataatt ctttcaactc 300

aatgttttag ccaaaactgc aaacatttga aatttaattt tgaataaaaa ttacagctta 360

tgcaccaaga taacattaga aagtgtcttc agacatttta tcaggtattt tcctcattac 420

acccaaccaa acacagaaag aaatatatat ttttgaaatg tcaattactg ctatgctatc 480

aaaagctgac at 492

<210> 99
<211> 275
<212> DNA
<213> Human

<400> 99
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ctgcttttat ctgaaagagg ggggaccact gttgtctcag tcacaaaaat tctgctgagt 180

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gcagaatgtg gcaaaagtgg ggctgctgct agctt 275

<210> 100
<211> 222
<212> DNA
<213> Human

<400> 100
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ggtattcggg catgagagca gcaggggcct cctgacgcgg gcaggagaaa catggcaccc 180

accaggagga ggaagaggag gaagaggata aggaggaagg tc 222

<210> 101
<211> 440
<212> DNA

<213> Human

<400> 101
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gtcttcccct cccaggaaag gactgttctt cagggctgtc ctcagattct tatttcatat 120

cttaaaaatg acatagtaaa aaagacctag atgtgatagt aaacccttat tttttaatat 180

accaaacagt tgtaaccaca aaagcactgt aatcatcatt tcttggaaaa gttataagca 240

tatttgaaac ttgaaacttc taaaatcttg gttagagaag aaaactaaat tctacattta 300

gtggaattaa gcttctacct aatagctttt ataccaactt tccaaaagta ggagtggtac 360

caggtttcca tgtaaaccca agaaagcagt ttatccatcc acacagccca acccttgctc 420

caatgagcat attactgggt 440

<210> 102
<211> 559
<212> DNA
<213> Human

<220>
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<222> (548)..(548)
<223> n is a, c, g, or t

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gagtctcact ctgtcgccca ggctggagtg cagtggccag atctcagctc actgaaacct 180

cagcctccca agttcaagtg attctcgtac ctcagcctcc tgagtagctg gaattccagg 240

ctgtactcac tgctttgctc atatccccgc tcattaccag ggacaggcca gcacccctgg 300

cattgcatct cacatatcca ctgatggatg gagaacagac tgaaattcag tgccttagag 360

accacacact ccaacccccct cattgtgcag atgggaaaac tgagagccat agaagggaag 420

tggcttgccc aaagccacac ttactgtttt ccccacactg taccacaaac tttcaccatt 480

cttcaggttt ggaaaaatac taataaactg atcaacacta aaaaaaaaaa agcggccgct 540

cggttgtngc gcggccggg 559

<210> 103
<211> 388
<212> DNA
<213> Human

<400> 103

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atttatatgg cttcattttc ttacatttgg atcctggatc cagatggagt tcattcttgc 180

atatggtgtg aagtacaggt ctaacttcaa ctttctccaa ggggctttcc agttggctca 240

gcaccattta ttaaagtctg ctttgacctg cgattgaaga tgccaccttt aactcctcat 300

cccccacccc taagaaacct cacggaacat atgacccaag agcagagcag acataaaaag 360

attaactgag ctactgagat tcggtcaa 388

<210> 104
<211> 545
<212> DNA
<213> Human

<400> 104
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agcaaattgc actcagatta aaataacaaa ataatctctt atcagaagct aagaaataca 180

ttttcctcct cctcatccat atccaaagac ggttctgaaa atgccttttc ttctctatta 240

tagcaacacc tagtggcttg agaaggccag gtctagaggt atgcatttac ggctgggaaa 300

cactgacctt tagctttgaa gacctcaggt agcacctaga cgtcggctat aaccgcataa 360

caatggtccc catctgaaac catttaagtc agaatctttg gaggaagagg ccaggattgg 420

taggttataa aagttgccca gatgatttta atgtgcagcc aaggctaaga gctacttatc 480

tagaccagtg gtttgcaaac ttttgtcaaa taatcagaat cgcgtgtcaa acacagattg 540

ctggg 545

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<211> 580
<212> DNA
<213> Human

<400> 105
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ggctgataga gaatcatgtg taactggggt cagcattcct ataatttttt gagccaaaga 180

cagaatacac actttaccct gacaggtttc ttccagaatt taggacagct gatgaaatga 240

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atgcctcata ccctcagacg tcccaaatcc agtggtgagc aggtaaattt ttaacaacaa 360

tctttctttg tgaggaaaaa agttcctgat ttccataatg taaatacttt cactgactgg 420

tttgaagcca tcaacacgtc aactaacaat tggttcctgc atgtctataa gctggcttta 480

gcacaccact gcaaacctac ttattactta tattttcaga tacattacag cacttatcaa 540

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<210> 106
<211> 618
<212> DNA
<213> Human

<400> 106
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aagagtttac atcataatta tataattgta tttttaaaca tcacagaaac ccaacatgta 240

cctatttgta atcatcagag tatatacatc tgattaggac tcagctatgt tcaaggcttc 300

atcgagccca acatacaatt atcatttgca ttttctgcta caatcaaaga aaacacattg 360

tgtgctatta gtggccattg caagaaggaa gatgctgttt tcaataacag gaaatcaaga 420

acaaacaaaa taatcgtctt ccatttaaaa aaaaaagaaa gcctacagaa aagtgaaaag 480

gacagggtcc taaaaacatc tagtgatgcc aataaaatgg aatgtttttt aaaaagtgat 540

ttgtctcact gaagctgcag aagggtatcc cacacttata tattatgtga ctgcactaaa 600

aacagacgct tttggtgc 618

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<211> 538
<212> DNA
<213> Human

<400> 107
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aaagttttcc ttggcttttg gttatgggct gtctgctgaa tatgagtctt ggatcttttt 180

cagcatcaac ttgcaaaagc tatgcctttc caccccttgcc cttgtagctt ttttgagtcc 240

aggtctcccc actcccatgc caatggaccc tttataatgg ggaaggcatc acagcaagac 300

gcaggcttgg ggctttccca atgaccaggt tctcattaag tgccatctca ccatcaacca 360

gcgacagcaa tgtccctttt gcccaagctc ctcctttccc tgcactctgg ttgccctcta 420

aatggcacca gcccaaacca gggacagtca ctcgtccact cacttcccaa atatttacag 480

agcgcctgtt gggtgccagg ctcctccagg ggccctgctg ccaggccgaa gcccacgg 538

<210> 108
<211> 542
<212> DNA
<213> Human

<400> 108
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aattaatttc tggccacaaa ttctattttt acagcatgta attgaaacca gattaccttt 180

ggtttttcta agccaccccc tccaccccta gagagggggc taaaaagaat gtagtataag 240

tgaatcttga aagatatcct tggattctgc tgtctcaaat acagtttgct gcaaaaagtc 300

tttgccaact aaactatcat taccttcccc gatgctaagg ttgaaaatca gcatcttgat 360

tataagccta actttcaagt ttctaactca gctgcaaaat attttcccaa ctaaacctgt 420

ggtgttccaa aaatatatac tatacagcaa tttctaaagt tataaatgtc ttggcgcatt 480

tggcatactt gcttaattcc aaaatcatta aaaagacaca tttagtgaaa aagtatctca 540

ca 542

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<211> 484
<212> DNA
<213> Human

<400> 109
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catgtagttt tcttctttct ctgtgttcta ttttattatt gtaaccactt tggtcttttt 180

ttttgtataa tcaattgcag ctagaatggt gtatggctct taatagatat tttggataat 240

gctgagtccc agaaatgtga agcctttccc gagtattgag ttcattaaag gttattatca 300

tcgtgtttaa tcagtaagtg attttaactt tcttcattat cccctcctct tgtttaactg 360

tggataagta gttcccatgg attgcttcct ctgtcttctt agcgagaaat atcggtggct 420

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<211> 478

<212> DNA
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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<222> (365)..(365)
<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<222> (402)..(402)
<223> n is a, c, g, or t

<220>
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<222> (439)..(439)
<223> n is a, c, g, or t

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<221> misc_feature
<222> (457)..(457)
<223> n is a, c, g, or t

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<222> (474)..(474)
<223> n is a, c, g, or t

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aaaacaaatg gagtgggnca caggaattnt cagaaatgga ggcttaggct gtccatacag 120

gattcagcaa gtacttgggg actgcgacta gaagaagcca gggtngggan taagtagctg 180

aggaggagag ggagctgatn tggaggagag caagggcaac ttcaaggaac aaaagggaag 240

ctgcaagnac cagctccatt aattcagcan acattccttg tctgtatgcc atgccagggt 300

ccttgttcta tggttctctc agtggggtag ctagaaactt gcccaacaga caggaacagn 360

cagangccaa agcaaagant tcctnaaagg tagccggcct gntgccaaac ctggggacaa 420

actttatgga ggcgccgtnt tttagccaga ccccgantta aaccttggtc ccancctg 478

<210> 111
<211> 313
<212> DNA
<213> Human

<400> 111
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ccaaagttga ttgtgacggg aagagggagg cccggtcgcc agctccaggc ctggcaacgc 120

ggcccgcccc gccgaccccc tacaaaagcc ctctgcccac cccccaccac cgggcgtgcc 180

tcgagccgcc ggccggcggt acaacaatat atatttatat ataatatata taaaacacag 240

agtcaggaaa ggcgggtaga aatatgaaat ccgtataaat gtgttgtttc cttcattaaa 300

gtgtcttcgg gga 313

<210> 112
<211> 498
<212> DNA
<213> Human

<400> 112
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cttaggtttt tactgctccc attcttgctt ttactaattt atccaagatt agatgtgatt 180

actatttaat aataatttag tcctcacact tacaaaccac ttacaatacc agcatgcttc 240

tatcactgta attctattca attctcaggc ccatgaggca tgccagccag acgaccagac 300

agcatttatt gagtgcccac tctataccag ccacaaaaga tcctgtgtca gaaggggaaa 360

caggcttgga ggcttggagt atgtacgtga tagcctccct cccagtccac acaactggta 420

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tgtgcttctc acgttgcc 498

<210> 113
<211> 590
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (450)..(450)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (515)..(515)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (547)..(547)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (558)..(558)
<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<222> (581)..(581)
<223> n is a, c, g, or t

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aatgatgtac atttatgaac gacgactaga agtgaacatg aataactgaa aacaaacagt 180

gtgatgcaag tgaatttttg gagggtgaga tggtcattat attgttcttc gagcaattaa 240

atattttatt ttcttcccaa aacaatgtcc acaagggggc agacagaaga tgacaaataa 300

aaccatttaa taaaaacctc agctgaaaag ctaataactc cagaatgcag gttgaaagca 360

agcttaaagg tcatctaggc tggggtcagt agctcacgcc tgcaatccca acaccctggg 420

aggcccaggt gagaggaccg ctcgagcccn ggaggtaaag gccgcagcga gctatgaccg 480

cgccactgca caccagcctg tgccacaaag taganttcgt cccaaaaaaa aaaaatcctc 540

ctagtcntct agtccatntc cccccctggn caagaaggac ngaggcccca 590

<210> 114
<211> 365
<212> DNA
<213> Human

<400> 114
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gagaatatat tgtaatgttc cataagtcat aacttaagga ccgagaatat attgcaatgt 120

tccataagtc ataatttaat gtgcagtaag aacccatgaa gttgtctgac caaaagtaac 180

actcttctgt tgggaaagat tttacatcct tttattctgg atgaatcctg aattctagat 240

gttgggttta atgcttcaca caatggcaca tttacaagag gtacaaaaca cttattgagc 300

tttcagggcc actgtaaggg gcttgcagaa tagcctcttt gcaacccaga gaattaatct 360

gattc 365

<210> 115
<211> 539
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (359)..(359)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (481)..(481)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (483)..(483)
<223> n is a, c, g, or t

<400> 115
tttttttttt tttagttttt ggtgattatt taattgcaga agctattatg atataattac 60

ttctggtgga ttaagtgctg cttaaatact aagactatcc attcactttt gcctcacgcc 120

tctctactaa actgcagctc agttctgcct ctcataatat gtatgttgag taacattatg 180

accacacagt gctcatcaaa aactattgct ccagctgtaa ttttaaatgt tggaggtggt 240

tcaaaattct aaagagttat agaaataaca cacatttgac aaatacatat aaaaatagtt 300

ataacatatt gaaatcacat taaaatatga aaaacccaca aagcataatt gcatcatant 360

atttgtgttg ctagacactg tccatctatt tttagaaaac gtcttaaatg tcactcaatg 420

gggcaacttt cctggtttcc tatgtcttac cttagaagca agcagtgtgt tagaatggat 480

ntnccatgca cgttagaccc caagatacaa caagcttctc tatacagaag ccatccatg 539

<210> 116
<211> 602
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (294)..(294)
<223> n is a, c, g, or t

<400> 116
ttccagtgtt tgaaccatct ttatttaatg aattattgat atcctttttt gtttccaaat 60

taaaacttca ccacatattt tcagctaagg taaatctgct tggtccaaac aaaacaaaac 120

aaaacaaaac accagactgc aacaataaca ggaaaagatc ctcttcagtg atttatgttg 180

ttctcttact ttcataacta gtttgaatgc aaggctggta aagggataca cagagaatca 240

ttattttaaa taacaaaagc cattcaaaac tctctctacc tgtcaaggat gttntatgct 300

cccattctta tttgtttggc agtaaacata ccttgcccac agtcgccagc atcaaaccca 360

caggacaaga cattgcatgc ttggtcacag aacttatcag cgagccagga attcgcacat 420

ccctgattac agtaagagac actgtttatt cctccaccaa actgccaggg ctgtccaact 480

ccaatactcc cagtacctcc acctcctgca atatagcgac tccctccact gtttccagag 540

caatccccac catcccaatc gcaggctgaa ttatttacag ccttgtcaca atagccatcc 600

tt 602

<210> 117
<211> 351
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (341)..(341)
<223> n is a, c, g, or t

<400> 117
tttttcggcc tcagtctgtt ctcagaacat actccatcac ctggttccca gaactcagat 60

tgcgcagtgg tctcgtcatc atcggccagg actcacagtg cccgcggcag aggcctccct 120

agacctccct cccgtccagc ctcacccgct gcctactctc ctcacgcccc tgctccaggt 180

cccctggccc catttcgctc gccacgtttt cataatcctc tcaggctccg ggcaagcggc 240

gccgccccgca atgggacctg atcatataag gaaaatactg cgggctcatc cgggggctgc 300

aatggtaacc cgaaagcgcc ctagcctact acaatcaccg naccccaact g 351

<210> 118
<211> 462
<212> DNA
<213> Human

<400> 118
gctaagaaat aacttttatt aaaaatactg tgctagtact tatgcaatta cataatttta 60

actaaatatt gtccactgcc acaattcgca ttaccaaact catattacca aattttaggc 120

cttgatagag cctaaatgct tcagtcactt cagaccaata acttaattct gttttcacat 180

accttataca ctggcctacc aatagctctc aattcctgtc aatactttcc ccattctgca 240

aaaagagggc cccatcccca tccctaatca aaaccaatgt gttgtacctg aaactgcaaa 300

gattaatgct tttcgatgac cactaacttt tgaagcccga aggcctaact tttagacaac 360

taaagctaca cactgttaaa attcttgggc ttctgtctta ttcagcaagc tgactcagta 420

aaattaatac actgtatgaa aaaagctaac atacctacaa tc 462

<210> 119
<211> 332
<212> DNA
<213> Human

<400> 119
tttttttttt tttttttttt ttttggttta aaaataaatt tattttatta catgataata 60

ttgacagttt acataaacaa agttatttag tgtatgcaaa gcaactataa aatacatttt 120

gaaaagatat aaaaatcttt gaaattcttt cttgatatca gatctaccaa atttcgagag 180

ccaccattga tattttagga tcaaaacaaa atggcttgag agattttgtt ggtcagccaa 240

actcagtcca ggaaaaaaga aacattaaag cattgttttg tgtttttaaa agctctaatg 300

gatatttatt ccaagctcct ttcgtatcga ag 332

<210> 120
<211> 473
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (373)..(373)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (429)..(429)
<223> n is a, c, g, or t

<400> 120
ttttttttaa aatttcttcc agtttgggat tgtgtataca caaaaagctc aaaataaagc 60

aactctgcaa tataatctta aaataatggc tactggggga aattctatca caaccattga 120

aaataatggt gacttctcac ggagtctgtg gcatctgaga acccagttaa ttaaccaaag 180

tcttgctcat attagcctca gttacccaga ttaaagcagg aactccggcc ttccctggac 240

tgctgaaaac ccaacagatt ttctcaacat gctataagga aagagggaaa aattggtttc 300

agctcacacc tcatgggctg ggaagcttct gggaaggcct ccaggccagt ggcacactcc 360

ccaactttat ggntaaaagg aggggccaat tttcattccc cacaggcatt cacaaggagt 420

tcccacccnt ccaaccacac agtggttttg gacaccaagg ttcacccttt cct 473

<210> 121
<211> 525
<212> DNA
<213> Human

<400> 121
gagaggtgat ataatttatt tttcttttcc atccaaatta tcagtaacag tggctaaatg 60

gcaagatagg ctaaaaaact ctaagtgacc caattttaca aattaaagaa gtaagtaaac 120

attagaatga atacagttaa acaggagagg ctgggcacag tggctcacac ctgtaatccc 180

agtattatcc agtaaaagtt tagcaagcaa attcaaagaa gtctgttgtg caaccatagc 240

cctttgcagt agaatctgct atacagccta ttatgaggga tcaatttctt tctttcttct 300

tttttttttg agacagagtc ttgctctgtt gcccaacctg gaatgcagtg gggtgatctt 360

ggctcactgc aacctctgcc tcccaggttc aagcaattct cctgtctcag cctcccgagt 420

agctggatta caggtgtgca ccatcacacc cagctaattt ttgtattttt agtagagatg 480

gggtttcacc acattggtca ggctggtctc aaactcctga cctca 525

<210> 122
<211> 849
<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (598)..(598)
<223> n is a, c, g, or t

<400> 122
atatgtatat tttcctctga ttttatgact gatttacaaa ttaggagtgc aaatgggctg 60

ttccccgata gcatcttctg ggaagaatcc aaccaagata caaagcagat gatggtggat 120

cggcaaactc ttttctatga aaagaaaaac cagatatacc agggactgga aagcacctgc 180

ttgaaaattg atatgagcat gtctgaattt ttcccttata agagcctgag tattgtaaca 240

ggtctcttgc acaggggggtt gaaaaataaa aaaagaagtt aacataatta aaatgcttgg 300

acaaaacatt tgctttatat agattcttac aagtaatatt tgattaggta tcaaaatagg 360

tttaggcagg tggaagttct gaatttcaag gcaaataagg catgaagggt ggaacattgc 420

atctagggaa aataagagaa ataagtgaaa gtctgaccct acattgccaa ttctcagacc 480

aagtacaaag tattaggaat tttttatatc agctgacatc tttgtgctta cagtaaagcc 540

atattagatg cacacatagt gactttatta aatcaaatga gtgtgcagag cagagcanat 600

ctaattaggc tttctctttt agagttttct tattttactc ttattagctc cctccagttg 660

gtcatcaatt tcctatccta catcagatat ttacactatc agattctttg gtttaaaatc 720

ctcttccggt ttacatttta atttctgggg cgctaaacac atacttctgt cccggtctta 780

tccctctatt ggaattcccc acagcgtggg caaaaacgcg ggctcgaaaa atgggggggcc 840

ccttcccct 849

<210> 123
<211> 454

<212> DNA
<213> Human

<220>
<221> misc_feature
<222> (433)..(433)
<223> n is a, c, g, or t

<400> 123
ttgtgagcaa catcggctgt ttattcactt gtgtgtgagt gggctgagtc cgagaaaggg 60

gtcagcaaaa ggtggtggga ttatcattgg ttcttatagg tttgggatag gcggtgtagt 120

caggagcaat tttttacagg caggggatgg atattacaaa gtacattctc aagggtgggg 180

aggatgttac aaagtacatt cacaagggca gggagggtgt atcgtcacaa gggcagggag 240

gatgtattgt cacaagggtg gggaggaatg ttacaaagta cattcacaag gacaggagta 300

tcacaaagta cattatcaca agggtggggg aatgtcaccg tggcttgacc attagtgcag 360

ccagctccag aggaccttac caaaaagttt ccatacttgc acgtgttttc ctggtggcca 420

aaaatataaa acntttaatt tctgggattc cttt 454

<210> 124
<211> 485
<212> DNA
<213> Human

<400> 124
ttcagatttg acatgtcaat ctttatttaa gacaacaaaa gtttgtacac tctcatatta 60

agatatattt cctttctagt catattaaaa taatctcatt ttgttactca aaaagaatac 120

atagggaaga gaatgaacat aattcaagta gatagatttc taattggtta aaacagggtt 180

aaacaaatga tgttcaaaat atacttatta aagggaacag cacctagaaa taggcagtag 240

ggcaatgttc actttaagaa ttttatcaat aactagggca aagaacaaaa tcattatcaa 300

attttgaatt acacaaaagc aatggcctat taccttgtta acatttgata tttctatata 360

tcttcttctc tagttgaaat gggtaatgac ttgtattaca aggatgttac acattctaaa 420

atgatttaag ccaaaagatt atctttaata cattacttct agatataata tgtacttgat 480

gtctg 485

<210> 125
<211> 558
<212> DNA
<213> Human

<400> 125
ttttcagaca tgacagcatt tgacacactc ccttttaatt tattgcagaa ataatatgaa 60

catctgggaa aatgatagtg ctaaatatct cgtgaagtaa gtcattctta gaaagggatt 120

tgtgactttg aagtaatata taattagcaa gattttaaaa attattctta tgtactgaaa 180

ctcaaaacag actagcaaag tacctccaaa aaaaaaacta tcaaattaaa ctagaaaagt 240

atttccaaaa taaagacgac caaaaactag cctgagaata ctagttttct gttgctacaa 300

cacattacca caaacttagt ggcttaaaca caaatctatt atcttacagt tctgcagatt 360

agaggtccaa cacaggcttc actgggctaa aatcaaggtg ttggcagggc tgcgttcctt 420

ctgggaggct atggggaagt ttctgtttcc tttccagtct caattctacc ggctgcctgc 480

aactccctgg cttatggccc cttcctccat cttcaaagcc aggaatggtg catccctctc 540

taagcgttct ccctattt 558

<210> 126
<211> 508
<212> PRT
<213> Human

<400> 126

Met Gln Arg Leu Leu Thr Pro Val Lys Arg Ile Leu Gln Leu Thr Arg
1 5 10 15

Ala Val Gln Glu Thr Ser Leu Thr Pro Ala Arg Leu Leu Pro Val Ala
20 25 30

His Gln Arg Phe Ser Thr Ala Ser Ala Val Pro Leu Ala Lys Thr Asp
35 40 45

Thr Trp Pro Lys Asp Val Gly Ile Leu Ala Leu Glu Val Tyr Phe Pro
50 55 60

Ala Gln Tyr Val Asp Gln Thr Asp Leu Glu Lys Tyr Asn Asn Val Glu
65 70 75 80

Ala Gly Lys Tyr Thr Val Gly Leu Gly Gln Thr Arg Met Gly Phe Cys
85 90 95

Ser Val Gln Glu Asp Ile Asn Ser Leu Cys Leu Thr Val Val Gln Arg
100 105 110

Leu Met Glu Arg Ile Gln Leu Pro Trp Asp Ser Val Gly Arg Leu Glu
115 120 125

Val Gly Thr Glu Thr Ile Ile Asp Lys Ser Lys Ala Val Lys Thr Val
130 135 140

Leu Met Glu Leu Phe Gln Asp Ser Gly Asn Thr Asp Ile Glu Gly Ile
145 150 155 160

Asp Thr Thr Asn Ala Cys Tyr Gly Gly Thr Ala Ser Leu Phe Asn Ala
165 170 175

Ala Asn Trp Met Glu Ser Ser Ser Trp Asp Gly Arg Tyr Ala Met Val
180 185 190

Val Cys Gly Asp Ile Ala Val Tyr Pro Ser Gly Asn Ala Arg Pro Thr
195 200 205

Gly Gly Ala Gly Ala Val Ala Met Leu Ile Gly Pro Lys Ala Pro Leu
210 215 220

Ala Leu Glu Arg Gly Leu Arg Gly Thr His Met Glu Asn Val Tyr Asp
225 230 235 240

Phe Tyr Lys Pro Asn Leu Ala Ser Glu Tyr Pro Ile Val Asp Gly Lys
245 250 255

Leu Ser Ile Gln Cys Tyr Leu Arg Ala Leu Asp Arg Cys Tyr Thr Ser
260 265 270

Tyr Arg Lys Lys Ile Gln Asn Gln Trp Lys Gln Ala Gly Ser Asp Arg
275 280 285

Pro Phe Thr Leu Asp Asp Leu Gln Tyr Met Ile Phe His Thr Pro Phe
290 295 300

Cys Lys Met Val Gln Lys Ser Leu Ala Arg Leu Met Phe Asn Asp Phe
305 310 315 320

Leu Ser Ala Ser Ser Asp Thr Gln Thr Ser Leu Tyr Lys Gly Leu Glu
325 330 335

Ala Phe Gly Gly Leu Lys Leu Glu Asp Thr Tyr Thr Asn Lys Asp Leu
340 345 350

Asp Lys Ala Leu Leu Lys Ala Ser Gln Asp Met Phe Asp Lys Lys Thr
355 360 365

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Lys Ala Ser Leu Tyr Leu Ser Thr His Asn Gly Asn Met Tyr Thr Ser
    370                 375                 380

Ser Leu Tyr Gly Cys Leu Ala Ser Leu Leu Ser His His Ser Ala Gln
385                 390                 395                 400

Glu Leu Ala Gly Ser Arg Ile Gly Ala Phe Ser Tyr Gly Ser Gly Leu
                405                 410                 415

Ala Ala Ser Phe Phe Ser Phe Arg Val Ser Gln Asp Ala Ala Pro Gly
            420                 425                 430

Ser Pro Leu Asp Lys Leu Val Ser Ser Thr Ser Asp Leu Pro Lys Arg
        435                 440                 445

Leu Ala Ser Arg Lys Cys Val Ser Pro Glu Glu Phe Thr Glu Ile Met
    450                 455                 460

Asn Gln Arg Glu Gln Phe Tyr His Lys Val Asn Phe Ser Pro Pro Gly
465                 470                 475                 480

Asp Thr Asn Ser Leu Phe Pro Gly Thr Trp Tyr Leu Glu Arg Val Asp
                485                 490                 495

Glu Gln His Arg Arg Lys Tyr Ala Arg Arg Pro Val
            500                 505


<210>  127
<211>  396
<212>  PRT
<213>  Human

<400>  127

Met Val Ala Gly Thr Arg Cys Leu Leu Ala Leu Leu Leu Pro Gln Val
1               5                   10                  15

Leu Leu Gly Gly Ala Ala Gly Leu Val Pro Glu Leu Gly Arg Arg Lys
            20                  25                  30

Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser Ser Gln Pro Ser Asp Glu
        35                  40                  45

Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly Leu Lys
    50                  55                  60
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Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr Met Leu
65 70 75 80

Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala Pro Asp
85 90 95

His Arg Leu Glu Arg Ala Ala Ser Arg Ala Asn Thr Val Arg Ser Phe
100 105 110

His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly Lys Thr
115 120 125

Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu Glu Phe
130 135 140

Ile Thr Ser Ala Glu Leu Gln Val Phe Arg Glu Gln Met Gln Asp Ala
145 150 155 160

Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr Glu Ile
165 170 175

Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg Leu Leu
180 185 190

Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser Phe Asp
195 200 205

Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala Asn His
210 215 220

Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly Val Ser
225 230 235 240

Lys Arg His Val Arg Ile Ser Arg Ser Leu His Gln Asp Glu His Ser
245 250 255

Trp Ser Gln Ile Arg Pro Leu Leu Val Thr Phe Gly His Asp Gly Lys
260 265 270

Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
275 280 285

Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp
290 295 300

Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr
305 310 315 320

His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
325 330 335

Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val
340 345 350

Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
355 360 365

Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu Lys Asn
370 375 380

Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
385 390 395

<210> 128
<211> 219
<212> PRT
<213> Human

<400> 128

Met Ala Asp Lys Ala Lys Pro Ala Lys Ala Ala Asn Arg Thr Pro Pro
1 5 10 15

Lys Ser Pro Gly Asp Pro Ser Lys Asp Arg Ala Ala Lys Arg Leu Ser
20 25 30

Leu Glu Ser Glu Gly Ala Gly Glu Gly Ala Ala Ala Ser Pro Glu Leu
35 40 45

Ser Ala Leu Glu Glu Ala Phe Arg Arg Phe Ala Val His Gly Asp Ala
50 55 60

Arg Ala Thr Gly Arg Glu Met His Gly Lys Asn Trp Ser Lys Leu Cys
65 70 75 80

Lys Asp Cys Gln Val Ile Asp Gly Arg Asn Val Thr Val Thr Asp Val
85 90 95

Asp Ile Val Phe Ser Lys Ile Lys Gly Lys Ser Cys Arg Thr Ile Thr
100 105 110

Phe Glu Gln Phe Gln Glu Ala Leu Glu Glu Leu Ala Lys Lys Arg Phe
115 120 125

Lys Asp Lys Ser Ser Glu Glu Ala Val Arg Glu Val His Arg Leu Ile
130 135 140

Glu Gly Lys Ala Pro Ile Ile Ser Gly Val Thr Lys Ala Ile Ser Ser
145 150 155 160

Pro Thr Val Ser Arg Leu Thr Asp Thr Thr Lys Phe Thr Gly Ser His
165 170 175

Lys Glu Arg Phe Asp Pro Ser Gly Lys Gly Lys Gly Lys Ala Gly Arg
180 185 190

Val Asp Leu Val Asp Glu Ser Gly Tyr Val Ser Gly Tyr Lys His Ala
195 200 205

Gly Thr Tyr Asp Gln Lys Val Gln Gly Gly Lys
210 215

<210> 129
<211> 384
<212> PRT
<213> Human

<400> 129

Met Asp Cys Ser Asn Gly Ser Ala Glu Cys Thr Gly Glu Gly Gly Ser
1 5 10 15

Lys Glu Val Val Gly Thr Phe Lys Ala Lys Asp Leu Ile Val Thr Pro
20 25 30

Ala Thr Ile Leu Lys Glu Lys Pro Asp Pro Asn Asn Leu Val Phe Gly
35 40 45

Thr Val Phe Thr Asp His Met Leu Thr Val Glu Trp Ser Ser Glu Phe
50 55 60

Gly Trp Glu Lys Pro His Ile Lys Pro Leu Gln Asn Leu Ser Leu His
65 70 75 80

Pro Gly Ser Ser Ala Leu His Tyr Ala Val Glu Leu Phe Glu Gly Leu
85 90 95

Lys Ala Phe Arg Gly Val Asp Asn Lys Ile Arg Leu Phe Gln Pro Asn
100 105 110

Leu Asn Met Asp Arg Met Tyr Arg Ser Ala Val Arg Ala Thr Leu Pro
115 120 125

Val Phe Asp Lys Glu Glu Leu Leu Glu Cys Ile Gln Gln Leu Val Lys
130 135 140

Leu Asp Gln Glu Trp Val Pro Tyr Ser Thr Ser Ala Ser Leu Tyr Ile
145 150 155 160

Arg Pro Ala Phe Ile Gly Thr Glu Pro Ser Leu Gly Val Lys Lys Pro
165 170 175

Thr Lys Ala Leu Leu Phe Val Leu Leu Ser Pro Val Gly Pro Tyr Phe
180 185 190

Ser Ser Gly Thr Phe Asn Pro Val Ser Leu Trp Ala Asn Pro Lys Tyr
195 200 205

Val Arg Ala Trp Lys Gly Gly Thr Gly Asp Cys Lys Met Gly Gly Asn
210 215 220

Tyr Gly Ser Ser Leu Phe Ala Gln Cys Glu Asp Val Asp Asn Gly Cys
225 230 235 240

Gln Gln Val Leu Trp Leu Tyr Gly Arg Asp His Gln Ile Thr Glu Val
245 250 255

Gly Thr Met Asn Leu Phe Leu Tyr Trp Ile Asn Glu Asp Gly Glu Glu
260 265 270

Glu Leu Ala Thr Pro Pro Leu Asp Gly Ile Ile Leu Pro Gly Val Thr
275 280 285

Arg Arg Cys Ile Leu Asp Leu Ala His Gln Trp Gly Glu Phe Lys Val
290 295 300

Ser Glu Arg Tyr Leu Thr Met Asp Asp Leu Thr Thr Ala Leu Glu Gly
305 310 315 320

Asn Arg Val Arg Glu Met Phe Ser Ser Gly Thr Ala Cys Val Val Cys

325 330 335

Pro Val Ser Asp Ile Leu Tyr Lys Gly Glu Thr Ile His Ile Pro Thr
340 345 350

Met Glu Asn Gly Pro Lys Leu Ala Ser Arg Ile Leu Ser Lys Leu Thr
355 360 365

Asp Ile Gln Tyr Gly Arg Glu Glu Ser Asp Trp Thr Ile Val Leu Ser
370 375 380

<210> 130
<211> 158
<212> PRT
<213> Human

<400> 130

Met Ser His Gly Lys Gly Thr Asp Met Leu Pro Glu Ile Ala Ala Ala
1 5 10 15

Val Gly Phe Leu Ser Ser Leu Leu Arg Thr Arg Gly Cys Val Ser Glu
20 25 30

Gln Arg Leu Lys Val Phe Ser Gly Ala Leu Gln Glu Ala Leu Thr Glu
35 40 45

His Tyr Lys His His Trp Phe Pro Glu Lys Pro Ser Lys Gly Ser Gly
50 55 60

Tyr Arg Cys Ile Arg Ile Asn His Lys Met Asp Pro Ile Ile Ser Arg
65 70 75 80

Val Ala Ser Gln Ile Gly Leu Ser Gln Pro Gln Leu His Gln Leu Leu
85 90 95

Pro Ser Glu Leu Thr Leu Trp Val Asp Pro Tyr Glu Val Ser Tyr Arg
100 105 110

Ile Gly Glu Asp Gly Ser Ile Cys Val Leu Tyr Glu Glu Ala Pro Leu
115 120 125

Ala Ala Ser Cys Gly Leu Leu Thr Cys Lys Asn Gln Val Leu Leu Gly
130 135 140

Arg Ser Ser Pro Ser Lys Asn Tyr Val Met Ala Val Ser Ser

145 150 155

<210> 131
<211> 344
<212> PRT
<213> Human

<400> 131

Met Gly Pro Pro Ser Ala Pro Pro Cys Arg Leu His Val Pro Trp Lys
1 5 10 15

Glu Val Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
20 25 30

Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
35 40 45

Lys Glu Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly
50 55 60

Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val
65 70 75 80

Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser
85 90 95

Gly Arg Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val
100 105 110

Thr Gln Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp
115 120 125

Leu Val Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu
130 135 140

Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys
145 150 155 160

Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr
165 170 175

Leu Trp Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Arg Leu Gln
180 185 190

Leu Ser Asn Gly Asn Met Thr Leu Thr Leu Leu Ser Val Lys Arg Asn

195 200 205

Asp Ala Gly Ser Tyr Glu Cys Glu Ile Gln Asn Pro Ala Ser Ala Asn
210 215 220

Arg Ser Asp Pro Val Thr Leu Asn Val Leu Tyr Gly Pro Asp Val Pro
225 230 235 240

Thr Ile Ser Pro Ser Lys Ala Asn Tyr Arg Pro Gly Glu Asn Leu Asn
245 250 255

Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser Trp Phe
260 265 270

Ile Asn Gly Thr Phe Gln Gln Ser Thr Gln Glu Leu Phe Ile Pro Asn
275 280 285

Ile Thr Val Asn Asn Ser Gly Ser Tyr Met Cys Gln Ala His Asn Ser
290 295 300

Ala Thr Gly Leu Asn Arg Thr Thr Val Thr Met Ile Thr Val Ser Gly
305 310 315 320

Ser Ala Pro Val Leu Ser Ala Val Ala Thr Val Gly Ile Thr Ile Gly
325 330 335

Val Leu Ala Arg Val Ala Leu Ile
340

<210> 132
<211> 479
<212> PRT
<213> Human

<400> 132

Met Lys Ser Gln Gly Gln His Trp Tyr Ser Ser Ser Asp Lys Asn Cys
1 5 10 15

Lys Val Ser Phe Arg Glu Lys Leu Leu Ile Ile Asp Ser Asn Leu Gly
20 25 30

Val Gln Asp Val Glu Asn Leu Lys Phe Leu Cys Ile Gly Leu Val Pro
35 40 45

Asn Lys Lys Leu Glu Lys Ser Ser Ser Ala Ser Asp Val Phe Glu His

50 55 60

Leu Leu Ala Glu Asp Leu Leu Ser Glu Glu Asp Pro Phe Phe Leu Ala
65 70 75 80

Glu Leu Leu Tyr Ile Ile Arg Gln Lys Lys Leu Leu Gln His Leu Asn
85 90 95

Cys Thr Lys Glu Glu Val Glu Arg Leu Leu Pro Thr Arg Gln Arg Val
100 105 110

Ser Leu Phe Arg Asn Leu Leu Tyr Glu Leu Ser Glu Gly Ile Asp Ser
115 120 125

Glu Asn Leu Lys Asp Met Ile Phe Leu Leu Lys Asp Ser Leu Pro Lys
130 135 140

Thr Glu Met Thr Ser Leu Ser Phe Leu Ala Phe Leu Glu Lys Gln Gly
145 150 155 160

Lys Ile Asp Glu Asp Asn Leu Thr Cys Leu Glu Asp Leu Cys Lys Thr
165 170 175

Val Val Pro Lys Leu Leu Arg Asn Ile Glu Lys Tyr Lys Arg Glu Lys
180 185 190

Ala Ile Gln Ile Val Thr Pro Pro Val Asp Lys Glu Ala Glu Ser Tyr
195 200 205

Gln Gly Glu Glu Glu Leu Val Ser Gln Thr Asp Val Lys Thr Phe Leu
210 215 220

Glu Ala Leu Pro Arg Ala Ala Val Tyr Arg Met Asn Arg Asn His Arg
225 230 235 240

Gly Leu Cys Val Ile Val Asn Asn His Ser Phe Thr Ser Leu Lys Asp
245 250 255

Arg Gln Gly Thr His Lys Asp Ala Glu Ile Leu Ser His Val Phe Gln
260 265 270

Trp Leu Gly Phe Thr Val His Ile His Asn Asn Val Thr Lys Val Glu
275 280 285

Met Glu Met Val Leu Gln Lys Gln Lys Cys Asn Pro Ala His Ala Asp
    290   295   300

Gly Asp Cys Phe Val Phe Cys Ile Leu Thr His Gly Arg Phe Gly Ala
305   310   315   320

Val Tyr Ser Ser Asp Glu Ala Leu Ile Pro Ile Arg Glu Ile Met Ser
                325   330   335

His Phe Thr Ala Leu Gln Cys Pro Arg Leu Ala Glu Lys Pro Lys Leu
            340   345   350

Phe Phe Ile Gln Ala Cys Gln Gly Glu Glu Ile Gln Pro Ser Val Ser
        355   360   365

Ile Glu Ala Asp Ala Leu Asn Pro Glu Gln Ala Pro Thr Ser Leu Gln
    370   375   380

Asp Ser Ile Pro Ala Glu Ala Asp Phe Leu Leu Gly Leu Ala Thr Val
385   390   395   400

Pro Gly Tyr Val Ser Phe Arg His Val Glu Glu Gly Ser Trp Tyr Ile
                405   410   415

Gln Ser Leu Cys Asn His Leu Lys Lys Leu Val Pro Arg His Glu Asp
            420   425   430

Ile Leu Ser Ile Leu Thr Ala Val Asn Asp Asp Val Ser Arg Arg Val
        435   440   445

Asp Lys Gln Gly Thr Lys Lys Gln Met Pro Gln Pro Ala Phe Thr Leu
    450   455   460

Arg Lys Lys Leu Val Phe Pro Val Pro Leu Asp Ala Leu Ser Ile
465   470   475

<210> 133
<211> 509
<212> PRT
<213> Human

<400> 133

Met Thr Val Glu Gly Arg Leu Leu Val Pro Asp Arg Ile Asn Gly Thr
1   5   10   15

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Ala Asn Lys Met Asn Gly Ala Leu Asp His Ser Asp Gln Pro Asp Pro
            20                  25                  30

Asp Ala Ile Lys Met Phe Val Gly Gln Ile Pro Arg Ser Trp Ser Glu
        35                  40                  45

Lys Glu Leu Lys Glu Leu Phe Glu Pro Tyr Gly Ala Val Tyr Gln Ile
    50                  55                  60

Asn Val Leu Arg Asp Arg Ser Gln Asn Pro Pro Gln Ser Lys Gly Cys
65                  70                  75                  80

Cys Phe Val Thr Phe Tyr Thr Arg Lys Ala Ala Leu Glu Ala Gln Asn
                85                  90                  95

Ala Leu His Asn Ile Lys Thr Leu Pro Gly Met His His Pro Ile Gln
            100                 105                 110

Met Lys Pro Ala Asp Ser Glu Lys Ser Asn Ala Val Glu Asp Arg Lys
        115                 120                 125

Leu Phe Ile Gly Met Val Ser Lys Lys Cys Asn Glu Asn Asp Ile Arg
    130                 135                 140

Val Met Phe Ser Pro Phe Gly Gln Ile Glu Glu Cys Arg Ile Leu Arg
145                 150                 155                 160

Gly Pro Asp Gly Leu Ser Arg Gly Cys Ala Phe Val Thr Phe Ser Thr
                165                 170                 175

Arg Ala Met Ala Gln Asn Ala Ile Lys Ala Met His Gln Ser Gln Thr
            180                 185                 190

Met Glu Gly Cys Ser Ser Pro Ile Val Val Lys Phe Ala Asp Thr Gln
        195                 200                 205

Lys Asp Lys Glu Gln Arg Arg Leu Gln Gln Gln Leu Ala Gln Gln Met
    210                 215                 220

Gln Gln Leu Asn Thr Ala Thr Trp Gly Asn Leu Thr Gly Leu Gly Gly
225                 230                 235                 240

Leu Thr Pro Gln Tyr Leu Ala Leu Leu Gln Gln Ala Thr Ser Ser Ser
                245                 250                 255
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Asn Leu Gly Ala Phe Ser Gly Ile Gln Gln Met Ala Gly Met Asn Ala
260 265 270

Leu Gln Leu Gln Asn Leu Ala Thr Leu Ala Ala Ala Ala Ala Ala Ala
275 280 285

Gln Thr Ser Ala Thr Ser Thr Asn Ala Asn Pro Leu Ser Thr Thr Ser
290 295 300

Ser Ala Leu Gly Ala Leu Thr Ser Pro Val Ala Ala Ser Thr Pro Asn
305 310 315 320

Ser Thr Ala Gly Ala Ala Met Asn Ser Leu Thr Ser Leu Gly Thr Leu
325 330 335

Gln Gly Leu Ala Gly Ala Thr Val Gly Leu Asn Asn Ile Asn Ala Leu
340 345 350

Ala Val Ala Gln Met Leu Ser Gly Met Ala Ala Leu Asn Gly Gly Leu
355 360 365

Gly Ala Thr Gly Leu Thr Asn Gly Thr Ala Gly Thr Met Asp Ala Leu
370 375 380

Thr Gln Ala Tyr Ser Gly Ile Gln Gln Tyr Ala Ala Ala Ala Leu Pro
385 390 395 400

Thr Leu Tyr Ser Gln Ser Leu Leu Gln Gln Gln Ser Ala Ala Gly Ser
405 410 415

Gln Lys Glu Gly Pro Glu Gly Ala Asn Leu Phe Ile Tyr His Leu Pro
420 425 430

Gln Glu Phe Gly Asp Gln His Ile Leu Gln Met Phe Met Pro Phe Gly
435 440 445

Asn Val Ile Ser Ala Lys Val Phe Ile Asp Lys Gln Thr Asn Leu Ser
450 455 460

Lys Cys Phe Gly Phe Val Ser Tyr Asp Asn Pro Val Ser Ala Gln Ala
465 470 475 480

Ala Ile Gln Ala Met Asn Gly Phe Gln Ile Gly Met Lys Arg Leu Lys
485 490 495

Val Gln Leu Lys Arg Ser Lys Asn Asp Ser Lys Pro Tyr
500 505

<210> 134
<211> 141
<212> PRT
<213> Human

<400> 134

Met Ala Arg Pro Leu Cys Thr Leu Leu Leu Leu Met Ala Thr Leu Ala
1 5 10 15

Gly Ala Leu Ala Ser Ser Ser Lys Glu Glu Asn Arg Ile Ile Pro Gly
20 25 30

Gly Ile Tyr Asp Ala Asp Leu Asn Asp Glu Trp Val Gln Arg Ala Leu
35 40 45

His Phe Ala Ile Ser Glu Tyr Asn Lys Ala Thr Glu Asp Glu Tyr Tyr
50 55 60

Arg Arg Pro Leu Gln Val Leu Arg Ala Arg Glu Gln Thr Phe Gly Gly
65 70 75 80

Val Asn Tyr Phe Phe Asp Val Glu Val Gly Arg Thr Ile Cys Thr Lys
85 90 95

Ser Gln Pro Asn Leu Asp Thr Cys Ala Phe His Glu Gln Pro Glu Leu
100 105 110

Gln Lys Lys Gln Leu Cys Ser Phe Glu Ile Tyr Glu Val Pro Trp Glu
115 120 125

Asp Arg Met Ser Leu Val Asn Ser Arg Cys Gln Glu Ala
130 135 140

<210> 135
<211> 1480
<212> PRT
<213> Human

<400> 135

Met Gln Arg Ser Pro Leu Glu Lys Ala Ser Val Val Ser Lys Leu Phe
1 5 10 15

Phe Ser Trp Thr Arg Pro Ile Leu Arg Lys Gly Tyr Arg Gln Arg Leu
20 25 30

Glu Leu Ser Asp Ile Tyr Gln Ile Pro Ser Val Asp Ser Ala Asp Asn
35 40 45

Leu Ser Glu Lys Leu Glu Arg Glu Trp Asp Arg Glu Leu Ala Ser Lys
50 55 60

Lys Asn Pro Lys Leu Ile Asn Ala Leu Arg Arg Cys Phe Phe Trp Arg
65 70 75 80

Phe Met Phe Tyr Gly Ile Phe Leu Tyr Leu Gly Glu Val Thr Lys Ala
85 90 95

Val Gln Pro Leu Leu Leu Gly Arg Ile Ile Ala Ser Tyr Asp Pro Asp
100 105 110

Asn Lys Glu Glu Arg Ser Ile Ala Ile Tyr Leu Gly Ile Gly Leu Cys
115 120 125

Leu Leu Phe Ile Val Arg Thr Leu Leu Leu His Pro Ala Ile Phe Gly
130 135 140

Leu His His Ile Gly Met Gln Met Arg Ile Ala Met Phe Ser Leu Ile
145 150 155 160

Tyr Lys Lys Thr Leu Lys Leu Ser Ser Arg Val Leu Asp Lys Ile Ser
165 170 175

Ile Gly Gln Leu Val Ser Leu Leu Ser Asn Asn Leu Asn Lys Phe Asp
180 185 190

Glu Gly Leu Ala Leu Ala His Phe Val Trp Ile Ala Pro Leu Gln Val
195 200 205

Ala Leu Leu Met Gly Leu Ile Trp Glu Leu Leu Gln Ala Ser Ala Phe
210 215 220

Cys Gly Leu Gly Phe Leu Ile Val Leu Ala Leu Phe Gln Ala Gly Leu
225 230 235 240

Gly Arg Met Met Met Lys Tyr Arg Asp Gln Arg Ala Gly Lys Ile Ser
245 250 255

Glu Arg Leu Val Ile Thr Ser Glu Met Ile Glu Asn Ile Gln Ser Val
260 265 270

Lys Ala Tyr Cys Trp Glu Glu Ala Met Glu Lys Met Ile Glu Asn Leu
275 280 285

Arg Gln Thr Glu Leu Lys Leu Thr Arg Lys Ala Ala Tyr Val Arg Tyr
290 295 300

Phe Asn Ser Ser Ala Phe Phe Phe Ser Gly Phe Phe Val Val Phe Leu
305 310 315 320

Ser Val Leu Pro Tyr Ala Leu Ile Lys Gly Ile Ile Leu Arg Lys Ile
325 330 335

Phe Thr Thr Ile Ser Phe Cys Ile Val Leu Arg Met Ala Val Thr Arg
340 345 350

Gln Phe Pro Trp Ala Val Gln Thr Trp Tyr Asp Ser Leu Gly Ala Ile
355 360 365

Asn Lys Ile Gln Asp Phe Leu Gln Lys Gln Glu Tyr Lys Thr Leu Glu
370 375 380

Tyr Asn Leu Thr Thr Thr Glu Val Val Met Glu Asn Val Thr Ala Phe
385 390 395 400

Trp Glu Glu Gly Phe Gly Glu Leu Phe Glu Lys Ala Lys Gln Asn Asn
405 410 415

Asn Asn Arg Lys Thr Ser Asn Gly Asp Asp Ser Leu Phe Phe Ser Asn
420 425 430

Phe Ser Leu Leu Gly Thr Pro Val Leu Lys Asp Ile Asn Phe Lys Ile
435 440 445

Glu Arg Gly Gln Leu Leu Ala Val Ala Gly Ser Thr Gly Ala Gly Lys
450 455 460

Thr Ser Leu Leu Met Met Ile Met Gly Glu Leu Glu Pro Ser Glu Gly
465 470 475 480

Lys Ile Lys His Ser Gly Arg Ile Ser Phe Cys Ser Gln Phe Ser Trp

485 490 495

Ile Met Pro Gly Thr Ile Lys Glu Asn Ile Ile Phe Gly Val Ser Tyr
500 505 510

Asp Glu Tyr Arg Tyr Arg Ser Val Ile Lys Ala Cys Gln Leu Glu Glu
515 520 525

Asp Ile Ser Lys Phe Ala Glu Lys Asp Asn Ile Val Leu Gly Glu Gly
530 535 540

Gly Ile Thr Leu Ser Gly Gly Gln Arg Ala Arg Ile Ser Leu Ala Arg
545 550 555 560

Ala Val Tyr Lys Asp Ala Asp Leu Tyr Leu Leu Asp Ser Pro Phe Gly
565 570 575

Tyr Leu Asp Val Leu Thr Glu Lys Glu Ile Phe Glu Ser Cys Val Cys
580 585 590

Lys Leu Met Ala Asn Lys Thr Arg Ile Leu Val Thr Ser Lys Met Glu
595 600 605

His Leu Lys Lys Ala Asp Lys Ile Leu Ile Leu Asn Glu Gly Ser Ser
610 615 620

Tyr Phe Tyr Gly Thr Phe Ser Glu Leu Gln Asn Leu Gln Pro Asp Phe
625 630 635 640

Ser Ser Lys Leu Met Gly Cys Asp Ser Phe Asp Gln Phe Ser Ala Glu
645 650 655

Arg Arg Asn Ser Ile Leu Thr Glu Thr Leu His Arg Phe Ser Leu Glu
660 665 670

Gly Asp Ala Pro Val Ser Trp Thr Glu Thr Lys Lys Gln Ser Phe Lys
675 680 685

Gln Thr Gly Glu Phe Gly Glu Lys Arg Lys Asn Ser Ile Leu Asn Pro
690 695 700

Ile Asn Ser Ile Arg Lys Phe Ser Ile Val Gln Lys Thr Pro Leu Gln
705 710 715 720

Met Asn Gly Ile Glu Glu Asp Ser Asp Glu Pro Leu Glu Arg Arg Leu
725 730 735

Ser Leu Val Pro Asp Ser Glu Gln Gly Glu Ala Ile Leu Pro Arg Ile
740 745 750

Ser Val Ile Ser Thr Gly Pro Thr Leu Gln Ala Arg Arg Arg Gln Ser
755 760 765

Val Leu Asn Leu Met Thr His Ser Val Asn Gln Gly Gln Asn Ile His
770 775 780

Arg Lys Thr Thr Ala Ser Thr Arg Lys Val Ser Leu Ala Pro Gln Ala
785 790 795 800

Asn Leu Thr Glu Leu Asp Ile Tyr Ser Arg Arg Leu Ser Gln Glu Thr
805 810 815

Gly Leu Glu Ile Ser Glu Glu Ile Asn Glu Glu Asp Leu Lys Glu Cys
820 825 830

Leu Phe Asp Asp Met Glu Ser Ile Pro Ala Val Thr Thr Trp Asn Thr
835 840 845

Tyr Leu Arg Tyr Ile Thr Val His Lys Ser Leu Ile Phe Val Leu Ile
850 855 860

Trp Cys Leu Val Ile Phe Leu Ala Glu Val Ala Ala Ser Leu Val Val
865 870 875 880

Leu Trp Leu Leu Gly Asn Thr Pro Leu Gln Asp Lys Gly Asn Ser Thr
885 890 895

His Ser Arg Asn Asn Ser Tyr Ala Val Ile Ile Thr Ser Thr Ser Ser
900 905 910

Tyr Tyr Val Phe Tyr Ile Tyr Val Gly Val Ala Asp Thr Leu Leu Ala
915 920 925

Met Gly Phe Phe Arg Gly Leu Pro Leu Val His Thr Leu Ile Thr Val
930 935 940

Ser Lys Ile Leu His His Lys Met Leu His Ser Val Leu Gln Ala Pro
945 950 955 960

Met Ser Thr Leu Asn Thr Leu Lys Ala Gly Gly Ile Leu Asn Arg Phe
965 970 975

Ser Lys Asp Ile Ala Ile Leu Asp Asp Leu Leu Pro Leu Thr Ile Phe
980 985 990

Asp Phe Ile Gln Leu Leu Leu Ile Val Ile Gly Ala Ile Ala Val Val
995 1000 1005

Ala Val Leu Gln Pro Tyr Ile Phe Val Ala Thr Val Pro Val Ile
1010 1015 1020

Val Ala Phe Ile Met Leu Arg Ala Tyr Phe Leu Gln Thr Ser Gln
1025 1030 1035

Gln Leu Lys Gln Leu Glu Ser Glu Gly Arg Ser Pro Ile Phe Thr
1040 1045 1050

His Leu Val Thr Ser Leu Lys Gly Leu Trp Thr Leu Arg Ala Phe
1055 1060 1065

Gly Arg Gln Pro Tyr Phe Glu Thr Leu Phe His Lys Ala Leu Asn
1070 1075 1080

Leu His Thr Ala Asn Trp Phe Leu Tyr Leu Ser Thr Leu Arg Trp
1085 1090 1095

Phe Gln Met Arg Ile Glu Met Ile Phe Val Ile Phe Phe Ile Ala
1100 1105 1110

Val Thr Phe Ile Ser Ile Leu Thr Thr Gly Glu Gly Glu Gly Arg
1115 1120 1125

Val Gly Ile Ile Leu Thr Leu Ala Met Asn Ile Met Ser Thr Leu
1130 1135 1140

Gln Trp Ala Val Asn Ser Ser Ile Asp Val Asp Ser Leu Met Arg
1145 1150 1155

Ser Val Ser Arg Val Phe Lys Phe Ile Asp Met Pro Thr Glu Gly
1160 1165 1170

Lys Pro Thr Lys Ser Thr Lys Pro Tyr Lys Asn Gly Gln Leu Ser
1175 1180 1185

Lys Val Met Ile Ile Glu Asn Ser His Val Lys Lys Asp Asp Ile
1190 1195 1200

Trp Pro Ser Gly Gly Gln Met Thr Val Lys Asp Leu Thr Ala Lys
1205 1210 1215

Tyr Thr Glu Gly Gly Asn Ala Ile Leu Glu Asn Ile Ser Phe Ser
1220 1225 1230

Ile Ser Pro Gly Gln Arg Val Gly Leu Leu Gly Arg Thr Gly Ser
1235 1240 1245

Gly Lys Ser Thr Leu Leu Ser Ala Phe Leu Arg Leu Leu Asn Thr
1250 1255 1260

Glu Gly Glu Ile Gln Ile Asp Gly Val Ser Trp Asp Ser Ile Thr
1265 1270 1275

Leu Gln Gln Trp Arg Lys Ala Phe Gly Val Ile Pro Gln Lys Val
1280 1285 1290

Phe Ile Phe Ser Gly Thr Phe Arg Lys Asn Leu Asp Pro Tyr Glu
1295 1300 1305

Gln Trp Ser Asp Gln Glu Ile Trp Lys Val Ala Asp Glu Val Gly
1310 1315 1320

Leu Arg Ser Val Ile Glu Gln Phe Pro Gly Lys Leu Asp Phe Val
1325 1330 1335

Leu Val Asp Gly Gly Cys Val Leu Ser His Gly His Lys Gln Leu
1340 1345 1350

Met Cys Leu Ala Arg Ser Val Leu Ser Lys Ala Lys Ile Leu Leu
1355 1360 1365

Leu Asp Glu Pro Ser Ala His Leu Asp Pro Val Thr Tyr Gln Ile
1370 1375 1380

Ile Arg Arg Thr Leu Lys Gln Ala Phe Ala Asp Cys Thr Val Ile
1385 1390 1395

Leu Cys Glu His Arg Ile Glu Ala Met Leu Glu Cys Gln Gln Phe

1400 1405 1410

Leu Val Ile Glu Glu Asn Lys Val Arg Gln Tyr Asp Ser Ile Gln
1415 1420 1425

Lys Leu Leu Asn Glu Arg Ser Leu Phe Arg Gln Ala Ile Ser Pro
1430 1435 1440

Ser Asp Arg Val Lys Leu Phe Pro His Arg Asn Ser Ser Lys Cys
1445 1450 1455

Lys Ser Lys Pro Gln Ile Ala Ala Leu Lys Glu Glu Thr Glu Glu
1460 1465 1470

Glu Val Gln Asp Thr Arg Leu
1475 1480

<210> 136
<211> 502
<212> PRT
<213> Human

<400> 136

Met Leu Ala Ala Met Gly Ser Leu Ala Ala Ala Leu Trp Ala Val Val
1 5 10 15

His Pro Arg Thr Leu Leu Leu Gly Thr Val Ala Phe Leu Leu Ala Ala
20 25 30

Asp Phe Leu Lys Arg Arg Arg Pro Lys Asn Tyr Pro Pro Gly Pro Trp
35 40 45

Arg Leu Pro Phe Leu Gly Asn Phe Phe Leu Val Asp Phe Glu Gln Ser
50 55 60

His Leu Glu Val Gln Leu Phe Val Lys Lys Tyr Gly Asn Leu Phe Ser
65 70 75 80

Leu Glu Leu Gly Asp Ile Ser Ala Val Leu Ile Thr Gly Leu Pro Leu
85 90 95

Ile Lys Glu Ala Leu Ile His Met Asp Gln Asn Phe Gly Asn Arg Pro
100 105 110

Val Thr Pro Met Arg Glu His Ile Phe Lys Lys Asn Gly Leu Ile Met

115 120 125

Ser Ser Gly Gln Ala Trp Lys Glu Gln Arg Arg Phe Thr Leu Thr Ala
130 135 140

Leu Arg Asn Phe Gly Leu Gly Lys Lys Ser Leu Glu Glu Arg Ile Gln
145 150 155 160

Glu Glu Ala Gln His Leu Thr Glu Ala Ile Lys Glu Glu Asn Gly Gln
165 170 175

Pro Phe Asp Pro His Phe Lys Ile Asn Asn Ala Val Ser Asn Ile Ile
180 185 190

Cys Ser Ile Thr Phe Gly Glu Arg Phe Glu Tyr Gln Asp Ser Trp Phe
195 200 205

Gln Gln Leu Leu Lys Leu Leu Asp Glu Val Thr Tyr Leu Glu Ala Ser
210 215 220

Lys Thr Cys Gln Leu Tyr Asn Val Phe Pro Trp Ile Met Lys Phe Leu
225 230 235 240

Pro Gly Pro His Gln Thr Leu Phe Ser Asn Trp Lys Lys Leu Lys Leu
245 250 255

Phe Val Ser His Met Ile Asp Lys His Arg Lys Asp Trp Asn Pro Ala
260 265 270

Glu Thr Arg Asp Phe Ile Asp Ala Tyr Leu Lys Glu Met Ser Lys His
275 280 285

Thr Gly Asn Pro Thr Ser Ser Phe His Glu Glu Asn Leu Ile Cys Ser
290 295 300

Thr Leu Asp Leu Phe Phe Ala Gly Thr Glu Thr Thr Ser Thr Thr Leu
305 310 315 320

Arg Trp Ala Leu Leu Tyr Met Ala Leu Tyr Pro Glu Ile Gln Glu Lys
325 330 335

Val Gln Ala Glu Ile Asp Arg Val Ile Gly Gln Gly Gln Gln Pro Ser
340 345 350

Thr Ala Ala Arg Glu Ser Met Pro Tyr Thr Asn Ala Val Ile His Glu
355 360 365

Val Gln Arg Met Gly Asn Ile Ile Pro Leu Asn Val Pro Arg Glu Val
370 375 380

Thr Val Asp Thr Thr Leu Ala Gly Tyr His Leu Pro Lys Gly Thr Met
385 390 395 400

Ile Leu Thr Asn Leu Thr Ala Leu His Arg Asp Pro Thr Glu Trp Ala
405 410 415

Thr Pro Asp Thr Phe Asn Pro Asp His Phe Leu Glu Asn Gly Gln Phe
420 425 430

Lys Lys Arg Glu Ala Phe Met Pro Phe Ser Ile Gly Lys Arg Ala Cys
435 440 445

Leu Gly Glu Gln Leu Ala Arg Thr Glu Leu Phe Ile Phe Phe Thr Ser
450 455 460

Leu Met Gln Lys Phe Thr Phe Arg Pro Pro Asn Asn Glu Lys Leu Ser
465 470 475 480

Leu Lys Phe Arg Met Gly Ile Thr Ile Ser Pro Val Ser His Arg Leu
485 490 495

Cys Ala Val Pro Gln Val
500

<210> 137
<211> 766
<212> PRT
<213> Human

<400> 137

Met Lys Thr Pro Trp Arg Val Leu Leu Gly Leu Leu Gly Ala Ala Ala
1 5 10 15

Leu Val Thr Ile Ile Thr Val Pro Val Val Leu Leu Asn Lys Gly Thr
20 25 30

Asp Asp Ala Thr Ala Asp Ser Arg Lys Thr Tyr Thr Leu Thr Asp Tyr
35 40 45

```
Leu Lys Asn Thr Tyr Arg Leu Lys Leu Tyr Ser Leu Arg Trp Ile Ser
    50                  55                  60

Asp His Glu Tyr Leu Tyr Lys Gln Glu Asn Asn Ile Leu Val Phe Asn
65                  70                  75                  80

Ala Glu Tyr Gly Asn Ser Ser Val Phe Leu Glu Asn Ser Thr Phe Asp
                85                  90                  95

Glu Phe Gly His Ser Ile Asn Asp Tyr Ser Ile Ser Pro Asp Gly Gln
            100                 105                 110

Phe Ile Leu Leu Glu Tyr Asn Tyr Val Lys Gln Trp Arg His Ser Tyr
        115                 120                 125

Thr Ala Ser Tyr Asp Ile Tyr Asp Leu Asn Lys Arg Gln Leu Ile Thr
    130                 135                 140

Glu Glu Arg Ile Pro Asn Asn Thr Gln Trp Val Thr Trp Ser Pro Val
145                 150                 155                 160

Gly His Lys Leu Ala Tyr Val Trp Asn Asn Asp Ile Tyr Val Lys Ile
                165                 170                 175

Glu Pro Asn Leu Pro Ser Tyr Arg Ile Thr Trp Thr Gly Lys Glu Asp
            180                 185                 190

Ile Ile Tyr Asn Gly Ile Thr Asp Trp Val Tyr Glu Glu Glu Val Phe
        195                 200                 205

Ser Ala Tyr Ser Ala Leu Trp Trp Ser Pro Asn Gly Thr Phe Leu Ala
    210                 215                 220

Tyr Ala Gln Phe Asn Asp Thr Glu Val Pro Leu Ile Glu Tyr Ser Phe
225                 230                 235                 240

Tyr Ser Asp Glu Ser Leu Gln Tyr Pro Lys Thr Val Arg Val Pro Tyr
                245                 250                 255

Pro Lys Ala Gly Ala Val Asn Pro Thr Val Lys Phe Phe Val Val Asn
            260                 265                 270

Thr Asp Ser Leu Ser Ser Val Thr Asn Ala Thr Ser Ile Gln Ile Thr
        275                 280                 285
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Ala Pro Ala Ser Met Leu Ile Gly Asp His Tyr Leu Cys Asp Val Thr
    290                 295                 300

Trp Ala Thr Gln Glu Arg Ile Ser Leu Gln Trp Leu Arg Arg Ile Gln
305                 310                 315                 320

Asn Tyr Ser Val Met Asp Ile Cys Asp Tyr Asp Glu Ser Ser Gly Arg
                325                 330                 335

Trp Asn Cys Leu Val Ala Arg Gln His Ile Glu Met Ser Thr Thr Gly
            340                 345                 350

Trp Val Gly Arg Phe Arg Pro Ser Glu Pro His Phe Thr Leu Asp Gly
        355                 360                 365

Asn Ser Phe Tyr Lys Ile Ile Ser Asn Glu Glu Gly Tyr Arg His Ile
    370                 375                 380

Cys Tyr Phe Gln Ile Asp Lys Lys Asp Cys Thr Phe Ile Thr Lys Gly
385                 390                 395                 400

Thr Trp Glu Val Ile Gly Ile Glu Ala Leu Thr Ser Asp Tyr Leu Tyr
                405                 410                 415

Tyr Ile Ser Asn Glu Tyr Lys Gly Met Pro Gly Gly Arg Asn Leu Tyr
            420                 425                 430

Lys Ile Gln Leu Ser Asp Tyr Thr Lys Val Thr Cys Leu Ser Cys Glu
        435                 440                 445

Leu Asn Pro Glu Arg Cys Gln Tyr Tyr Ser Val Ser Phe Ser Lys Glu
    450                 455                 460

Ala Lys Tyr Tyr Gln Leu Arg Cys Ser Gly Pro Gly Leu Pro Leu Tyr
465                 470                 475                 480

Thr Leu His Ser Ser Val Asn Asp Lys Gly Leu Arg Val Leu Glu Asp
                485                 490                 495

Asn Ser Ala Leu Asp Lys Met Leu Gln Asn Val Gln Met Pro Ser Lys
            500                 505                 510

Lys Leu Asp Phe Ile Ile Leu Asn Glu Thr Lys Phe Trp Tyr Gln Met
        515                 520                 525
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Ile Leu Pro Pro His Phe Asp Lys Ser Lys Lys Tyr Pro Leu Leu Leu
530 535 540

Asp Val Tyr Ala Gly Pro Cys Ser Gln Lys Ala Asp Ile Val Phe Arg
545 550 555 560

Leu Asn Trp Ala Thr Tyr Leu Ala Ser Thr Glu Asn Ile Ile Val Ala
565 570 575

Ser Phe Asp Gly Arg Gly Ser Gly Tyr Gln Gly Asp Lys Ile Met His
580 585 590

Ala Ile Asn Arg Arg Leu Gly Thr Phe Glu Val Glu Asp Gln Ile Glu
595 600 605

Ala Ala Arg Gln Phe Ser Lys Met Gly Phe Val Asp Asn Lys Arg Ile
610 615 620

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Thr Ser Met Val Leu
625 630 635 640

Gly Ser Gly Ser Gly Val Phe Lys Cys Gly Ile Ala Val Ala Pro Val
645 650 655

Ser Arg Trp Glu Tyr Tyr Glu Ser Val Tyr Thr Glu Arg Tyr Met Gly
660 665 670

Leu Pro Thr Pro Glu Asp Asn Leu Asp His Tyr Arg Asn Ser Thr Val
675 680 685

Met Ser Arg Ala Glu Asn Phe Lys Gln Val Glu Tyr Leu Leu Ile His
690 695 700

Gly Thr Ala Asp Asp Asn Val His Phe Gln Gln Ser Ala Gln Ile Ser
705 710 715 720

Lys Ala Leu Val Asp Val Gly Val Asp Phe Gln Ala Met Trp Tyr Thr
725 730 735

Asp Glu Asp His Gly Ile Ala Ser Ser Thr Ala His Gln His Ile Tyr
740 745 750

Thr His Met Ser His Phe Ile Lys Gln Cys Phe Ser Leu Pro

755 760 765

<210> 138
<211> 984
<212> PRT
<213> Human

<400> 138

Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
1 5 10 15

Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
20 25 30

Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
35 40 45

Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
50 55 60

Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65 70 75 80

Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His
85 90 95

Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
100 105 110

Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
115 120 125

Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
130 135 140

Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Ala
145 150 155 160

Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
165 170 175

Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
180 185 190

Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu

195 200 205

Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
210 215 220

Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225 230 235 240

Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
245 250 255

Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
260 265 270

Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
275 280 285

Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
290 295 300

Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305 310 315 320

Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
325 330 335

Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
340 345 350

Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
355 360 365

Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
370 375 380

Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Ala Leu Thr
385 390 395 400

Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
405 410 415

Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
420 425 430

His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Glu Ser Leu
435 440 445

Ser Gly Leu Ser Leu Arg Leu Val Lys Lys Glu Pro Arg Gln Leu Glu
450 455 460

Leu Thr Trp Ala Gly Ser Arg Pro Arg Ser Pro Gly Ala Asn Leu Thr
465 470 475 480

Tyr Glu Leu His Val Leu Asn Gln Asp Glu Glu Arg Tyr Gln Met Val
485 490 495

Leu Glu Pro Arg Val Leu Leu Thr Glu Leu Gln Pro Asp Thr Thr Tyr
500 505 510

Ile Val Arg Val Arg Met Leu Thr Pro Leu Gly Pro Gly Pro Phe Ser
515 520 525

Pro Asp His Glu Phe Arg Thr Ser Pro Pro Val Ser Arg Gly Leu Thr
530 535 540

Gly Gly Glu Ile Val Ala Val Ile Phe Gly Leu Leu Leu Gly Ala Ala
545 550 555 560

Leu Leu Leu Gly Ile Leu Val Phe Arg Ser Arg Arg Ala Gln Arg Gln
565 570 575

Arg Gln Gln Arg His Val Thr Ala Pro Pro Met Trp Ile Glu Arg Thr
580 585 590

Ser Cys Ala Glu Ala Leu Cys Gly Thr Ser Arg His Thr Arg Thr Leu
595 600 605

His Arg Glu Pro Trp Thr Leu Pro Gly Gly Trp Ser Asn Phe Pro Ser
610 615 620

Arg Glu Leu Asp Pro Ala Trp Leu Met Val Asp Thr Val Ile Gly Glu
625 630 635 640

Gly Glu Phe Gly Glu Val Tyr Arg Gly Thr Leu Arg Leu Pro Ser Gln
645 650 655

Asp Cys Lys Thr Val Ala Ile Lys Thr Leu Lys Asp Thr Ser Pro Gly
660 665 670

```
Gly Gln Trp Trp Asn Phe Leu Arg Glu Ala Thr Ile Met Gly Gln Phe
        675                 680                 685

Ser His Pro His Ile Leu His Leu Glu Gly Val Val Thr Lys Arg Lys
    690                 695                 700

Pro Ile Met Ile Ile Thr Glu Phe Met Glu Asn Ala Ala Leu Asp Ala
705                 710                 715                 720

Phe Leu Arg Glu Arg Glu Asp Gln Leu Val Pro Gly Gln Leu Val Ala
                725                 730                 735

Met Leu Gln Gly Ile Ala Ser Gly Met Asn Tyr Leu Ser Asn His Asn
            740                 745                 750

Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Gln Asn
        755                 760                 765

Leu Cys Cys Lys Val Ser Asp Phe Gly Leu Thr Arg Leu Leu Asp Asp
    770                 775                 780

Phe Asp Gly Thr Tyr Glu Thr Gln Gly Gly Lys Ile Pro Ile Arg Trp
785                 790                 795                 800

Thr Ala Pro Glu Ala Ile Ala His Arg Ile Phe Thr Thr Ala Ser Asp
                805                 810                 815

Val Trp Ser Phe Gly Ile Val Met Trp Glu Val Leu Ser Phe Gly Asp
            820                 825                 830

Lys Pro Tyr Gly Glu Met Ser Asn Gln Glu Val Met Lys Ser Ile Glu
        835                 840                 845

Asp Gly Tyr Arg Leu Pro Pro Pro Val Asp Cys Pro Ala Pro Leu Tyr
    850                 855                 860

Glu Leu Met Lys Asn Cys Trp Ala Tyr Asp Arg Ala Arg Arg Pro His
865                 870                 875                 880

Phe Gln Lys Leu Gln Ala His Leu Glu Gln Leu Leu Ala Asn Pro His
                885                 890                 895

Ser Leu Arg Thr Ile Ala Asn Phe Asp Pro Arg Val Thr Leu Arg Leu
            900                 905                 910
```

Pro Ser Leu Ser Gly Ser Asp Gly Ile Pro Tyr Arg Thr Val Ser Glu
915 920 925

Trp Leu Glu Ser Ile Arg Met Lys Arg Tyr Ile Leu His Phe His Ser
930 935 940

Ala Gly Leu Asp Thr Met Glu Cys Val Leu Glu Leu Thr Ala Glu Asp
945 950 955 960

Leu Thr Gln Met Gly Ile Thr Leu Pro Gly His Gln Lys Arg Ile Leu
965 970 975

Cys Ser Ile Gln Gly Phe Lys Asp
980

<210> 139
<211> 822
<212> PRT
<213> Human

<400> 139

Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
1 5 10 15

Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
20 25 30

Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
35 40 45

Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
50 55 60

Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65 70 75 80

Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
85 90 95

Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
100 105 110

Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
115 120 125

Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
130 135 140

Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145 150 155 160

Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
165 170 175

Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
180 185 190

Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
195 200 205

Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
210 215 220

Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225 230 235 240

Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
245 250 255

Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
260 265 270

Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
275 280 285

Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
290 295 300

Gly Leu Pro Tyr Leu Lys Val Leu Lys His Ser Gly Ile Asn Ser Ser
305 310 315 320

Asn Ala Glu Val Leu Ala Leu Phe Asn Val Thr Glu Ala Asp Ala Gly
325 330 335

Glu Tyr Ile Cys Lys Val Ser Asn Tyr Ile Gly Gln Ala Asn Gln Ser
340 345 350

Ala Trp Leu Thr Val Leu Pro Lys Gln Gln Ala Pro Gly Arg Glu Lys

355 360 365

Glu Ile Thr Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile
370 375 380

Gly Val Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg
385 390 395 400

Met Lys Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val
405 410 415

His Lys Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser
420 425 430

Ala Glu Ser Ser Ser Ser Met Asn Ser Asn Thr Pro Leu Val Arg Ile
435 440 445

Thr Thr Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val
450 455 460

Ser Glu Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp
465 470 475 480

Lys Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val
485 490 495

Val Met Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala
500 505 510

Val Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp
515 520 525

Leu Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys
530 535 540

His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro
545 550 555 560

Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr
565 570 575

Leu Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn
580 585 590

Arg Val Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr
595 600 605

Tyr Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile
610 615 620

His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val
625 630 635 640

Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp
645 650 655

Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala
660 665 670

Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp
675 680 685

Ser Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro
690 695 700

Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly
705 710 715 720

His Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met
725 730 735

Met Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys
740 745 750

Gln Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu
755 760 765

Glu Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr
770 775 780

Pro Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser
785 790 795 800

Pro Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile
805 810 815

Asn Gly Ser Val Lys Thr
820

<210> 140
<211> 87
<212> PRT
<213> Human

<400> 140

Met Gln Lys Val Thr Leu Gly Leu Leu Val Phe Leu Ala Gly Phe Pro
1 5 10 15

Val Leu Asp Ala Asn Asp Leu Glu Asp Lys Asn Ser Pro Phe Tyr Tyr
20 25 30

Asp Trp His Ser Leu Gln Val Gly Gly Leu Ile Cys Ala Gly Val Leu
35 40 45

Cys Ala Met Gly Ile Ile Ile Val Met Ser Ala Lys Cys Lys Cys Lys
50 55 60

Phe Gly Gln Lys Ser Gly His His Pro Gly Glu Thr Pro Pro Leu Ile
65 70 75 80

Thr Pro Gly Ser Ala Gln Ser
85

<210> 141
<211> 907
<212> PRT
<213> Human

<400> 141

Met Asp Thr Ser Arg Leu Gly Val Leu Leu Ser Leu Pro Val Leu Leu
1 5 10 15

Gln Leu Ala Thr Gly Gly Ser Ser Pro Arg Ser Gly Val Leu Leu Arg
20 25 30

Gly Cys Pro Thr His Cys His Cys Glu Pro Asp Gly Arg Met Leu Leu
35 40 45

Arg Val Asp Cys Ser Asp Leu Gly Leu Ser Glu Leu Pro Ser Asn Leu
50 55 60

Ser Val Phe Thr Ser Tyr Leu Asp Leu Ser Met Asn Asn Ile Ser Gln
65 70 75 80

Leu Leu Pro Asn Pro Leu Pro Ser Leu Arg Phe Leu Glu Glu Leu Arg
85 90 95

Leu Ala Gly Asn Ala Leu Thr Tyr Ile Pro Lys Gly Ala Phe Thr Gly
100 105 110

Leu Tyr Ser Leu Lys Val Leu Met Leu Gln Asn Asn Gln Leu Arg His
115 120 125

Val Pro Thr Glu Ala Leu Gln Asn Leu Arg Ser Leu Gln Ser Leu Arg
130 135 140

Leu Asp Ala Asn His Ile Ser Tyr Val Pro Pro Ser Cys Phe Ser Gly
145 150 155 160

Leu His Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu
165 170 175

Ile Pro Val Gln Ala Phe Arg Ser Leu Ser Ala Leu Gln Ala Met Thr
180 185 190

Leu Ala Leu Asn Lys Ile His His Ile Pro Asp Tyr Ala Phe Gly Asn
195 200 205

Leu Ser Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile His Ser
210 215 220

Leu Gly Lys Lys Cys Phe Asp Gly Leu His Ser Leu Glu Thr Leu Asp
225 230 235 240

Leu Asn Tyr Asn Asn Leu Asp Glu Phe Pro Thr Ala Ile Arg Thr Leu
245 250 255

Ser Asn Leu Lys Glu Leu Gly Phe His Ser Asn Asn Ile Arg Ser Ile
260 265 270

Pro Glu Lys Ala Phe Val Gly Asn Pro Ser Leu Ile Thr Ile His Phe
275 280 285

Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln His Leu
290 295 300

Pro Glu Leu Arg Thr Leu Thr Leu Asn Gly Ala Ser Gln Ile Thr Glu
305 310 315 320

Phe Pro Asp Leu Thr Gly Thr Ala Asn Leu Glu Ser Leu Thr Leu Thr
325 330 335

Gly Ala Gln Ile Ser Ser Leu Pro Gln Thr Val Cys Asn Gln Leu Pro
340 345 350

Asn Leu Gln Val Leu Asp Leu Ser Tyr Asn Leu Leu Glu Asp Leu Pro
355 360 365

Ser Phe Ser Val Cys Gln Lys Leu Gln Lys Ile Asp Leu Arg His Asn
370 375 380

Glu Ile Tyr Glu Ile Lys Val Asp Thr Phe Gln Gln Leu Leu Ser Leu
385 390 395 400

Arg Ser Leu Asn Leu Ala Trp Asn Lys Ile Ala Ile Ile His Pro Asn
405 410 415

Ala Phe Ser Thr Leu Pro Ser Leu Ile Lys Leu Asp Leu Ser Ser Asn
420 425 430

Leu Leu Ser Ser Phe Pro Ile Thr Gly Leu His Gly Leu Thr His Leu
435 440 445

Lys Leu Thr Gly Asn His Ala Leu Gln Ser Leu Ile Ser Ser Glu Asn
450 455 460

Phe Pro Glu Leu Lys Val Ile Glu Met Pro Tyr Ala Tyr Gln Cys Cys
465 470 475 480

Ala Phe Gly Val Cys Glu Asn Ala Tyr Lys Ile Ser Asn Gln Trp Asn
485 490 495

Lys Gly Asp Asn Ser Ser Met Asp Asp Leu His Lys Lys Asp Ala Gly
500 505 510

Met Phe Gln Ala Gln Asp Glu Arg Asp Leu Glu Asp Phe Leu Leu Asp
515 520 525

Phe Glu Glu Asp Leu Lys Ala Leu His Ser Val Gln Cys Ser Pro Ser
530 535 540

Pro Gly Pro Phe Lys Pro Cys Glu His Leu Leu Asp Gly Trp Leu Ile
545 550 555 560

Arg Ile Gly Val Trp Thr Ile Ala Val Leu Ala Leu Thr Cys Asn Ala
565 570 575

Leu Val Thr Ser Thr Val Phe Arg Ser Pro Leu Tyr Ile Ser Pro Ile
580 585 590

Lys Leu Leu Ile Gly Val Ile Ala Ala Val Asn Met Leu Thr Gly Val
595 600 605

Ser Ser Ala Val Leu Ala Gly Val Asp Ala Phe Thr Phe Gly Ser Phe
610 615 620

Ala Arg His Gly Ala Trp Trp Glu Asn Gly Val Gly Cys His Val Ile
625 630 635 640

Gly Phe Leu Ser Ile Phe Ala Ser Glu Ser Ser Val Phe Leu Leu Thr
645 650 655

Leu Ala Ala Leu Glu Arg Gly Phe Ser Val Lys Tyr Ser Ala Lys Phe
660 665 670

Glu Thr Lys Ala Pro Phe Ser Ser Leu Lys Val Ile Ile Leu Leu Cys
675 680 685

Ala Leu Leu Ala Leu Thr Met Ala Ala Val Pro Leu Leu Gly Gly Ser
690 695 700

Lys Tyr Gly Ala Ser Pro Leu Cys Leu Pro Leu Pro Phe Gly Glu Pro
705 710 715 720

Ser Thr Met Gly Tyr Met Val Ala Leu Ile Leu Leu Asn Ser Leu Cys
725 730 735

Phe Leu Met Met Thr Ile Ala Tyr Thr Lys Leu Tyr Cys Asn Leu Asp
740 745 750

Lys Gly Asp Leu Glu Asn Ile Trp Asp Cys Ser Met Val Lys His Ile
755 760 765

Ala Leu Leu Leu Phe Thr Asn Cys Ile Leu Asn Cys Pro Val Ala Phe
770 775 780

Leu Ser Phe Ser Ser Leu Ile Asn Leu Thr Phe Ile Ser Pro Glu Val

785 790 795 800

Ile Lys Phe Ile Leu Leu Val Val Val Pro Leu Pro Ala Cys Leu Asn
805 810 815

Pro Leu Leu Tyr Ile Leu Phe Asn Pro His Phe Lys Glu Asp Leu Val
820 825 830

Ser Leu Arg Lys Gln Thr Tyr Val Trp Thr Arg Ser Lys His Pro Ser
835 840 845

Leu Met Ser Ile Asn Ser Asp Asp Val Glu Lys Gln Ser Cys Asp Ser
850 855 860

Thr Gln Ala Leu Val Thr Phe Thr Ser Ser Ser Ile Thr Tyr Asp Leu
865 870 875 880

Pro Pro Ser Ser Val Pro Ser Pro Ala Tyr Pro Val Thr Glu Ser Cys
885 890 895

His Leu Ser Ser Val Ala Phe Val Pro Cys Leu
900 905

<210> 142
<211> 1134
<212> PRT
<213> Human

<400> 142

Met Glu Ser Thr Pro Ser Phe Leu Lys Gly Thr Pro Thr Trp Glu Lys
1 5 10 15

Thr Ala Pro Glu Asn Gly Ile Val Arg Gln Glu Pro Gly Ser Pro Pro
20 25 30

Arg Asp Gly Leu His His Gly Pro Leu Cys Leu Gly Glu Pro Ala Pro
35 40 45

Phe Trp Arg Gly Val Leu Ser Thr Pro Asp Ser Trp Leu Pro Pro Gly
50 55 60

Phe Pro Gln Gly Pro Lys Asp Met Leu Pro Leu Val Glu Gly Glu Gly
65 70 75 80

Pro Gln Asn Gly Glu Arg Lys Val Asn Trp Leu Gly Ser Lys Glu Gly

85 90 95

Leu Arg Trp Lys Glu Ala Met Leu Thr His Pro Leu Ala Phe Cys Gly
100 105 110

Pro Ala Cys Pro Pro Arg Cys Gly Pro Leu Met Pro Glu His Ser Gly
115 120 125

Gly His Leu Lys Ser Asp Pro Val Ala Phe Arg Pro Trp His Cys Pro
130 135 140

Phe Leu Leu Glu Thr Lys Ile Leu Glu Arg Ala Pro Phe Trp Val Pro
145 150 155 160

Thr Cys Leu Pro Pro Tyr Leu Val Ser Gly Leu Pro Pro Glu His Pro
165 170 175

Cys Asp Trp Pro Leu Thr Pro His Pro Trp Val Tyr Ser Gly Gly Gln
180 185 190

Pro Lys Val Pro Ser Ala Phe Ser Leu Gly Ser Lys Gly Phe Tyr Tyr
195 200 205

Lys Asp Pro Ser Ile Pro Arg Leu Ala Lys Glu Pro Leu Ala Ala Ala
210 215 220

Glu Pro Gly Leu Phe Gly Leu Asn Ser Gly Gly His Leu Gln Arg Ala
225 230 235 240

Gly Glu Ala Glu Arg Pro Ser Leu His Gln Arg Asp Gly Glu Met Gly
245 250 255

Ala Gly Arg Gln Gln Asn Pro Cys Pro Leu Phe Leu Gly Gln Pro Asp
260 265 270

Thr Val Pro Trp Thr Ser Trp Pro Ala Cys Pro Pro Gly Leu Val His
275 280 285

Thr Leu Gly Asn Val Trp Ala Gly Pro Gly Asp Gly Asn Leu Gly Tyr
290 295 300

Gln Leu Gly Pro Pro Ala Thr Pro Arg Cys Pro Ser Pro Glu Pro Pro
305 310 315 320

Val Thr Gln Arg Gly Cys Cys Ser Ser Tyr Pro Pro Thr Lys Gly Gly
325 330 335

Gly Leu Gly Pro Cys Gly Lys Cys Gln Glu Gly Leu Glu Gly Gly Ala
340 345 350

Ser Gly Ala Ser Glu Pro Ser Glu Glu Val Asn Lys Ala Ser Gly Pro
355 360 365

Arg Ala Cys Pro Pro Ser His His Thr Lys Leu Lys Lys Thr Trp Leu
370 375 380

Thr Arg His Ser Glu Gln Phe Glu Cys Pro Arg Gly Cys Pro Glu Val
385 390 395 400

Glu Glu Arg Pro Val Ala Arg Leu Arg Ala Leu Lys Arg Ala Gly Ser
405 410 415

Pro Glu Val Gln Gly Ala Met Gly Ser Pro Ala Pro Lys Arg Pro Pro
420 425 430

Asp Pro Phe Pro Gly Thr Ala Glu Gln Gly Ala Gly Gly Trp Gln Glu
435 440 445

Val Arg Asp Thr Ser Ile Gly Asn Lys Asp Val Asp Ser Gly Gln His
450 455 460

Asp Glu Gln Lys Gly Pro Gln Asp Gly Gln Ala Ser Leu Gln Asp Pro
465 470 475 480

Gly Leu Gln Asp Ile Pro Cys Leu Ala Leu Pro Ala Lys Leu Ala Gln
485 490 495

Cys Gln Ser Cys Ala Gln Ala Ala Gly Glu Gly Gly Gly His Ala Cys
500 505 510

His Ser Gln Gln Val Arg Arg Ser Pro Leu Gly Gly Glu Leu Gln Gln
515 520 525

Glu Glu Asp Thr Ala Thr Asn Ser Ser Ser Glu Glu Gly Pro Gly Ser
530 535 540

Gly Pro Asp Ser Arg Leu Ser Thr Gly Leu Ala Lys His Leu Leu Ser
545 550 555 560

```
Gly Leu Gly Asp Arg Leu Cys Arg Leu Leu Arg Arg Glu Arg Glu Ala
                565                 570                 575

Leu Ala Trp Ala Gln Arg Glu Gly Gln Gly Pro Ala Val Thr Glu Asp
            580                 585                 590

Ser Pro Gly Ile Pro Arg Cys Cys Ser Arg Cys His His Gly Leu Phe
        595                 600                 605

Asn Thr His Trp Arg Cys Pro Arg Cys Ser His Arg Leu Cys Val Ala
    610                 615                 620

Cys Gly Arg Val Ala Gly Thr Gly Arg Ala Arg Glu Lys Ala Gly Phe
625                 630                 635                 640

Gln Glu Gln Ser Ala Glu Glu Cys Thr Gln Glu Ala Gly His Ala Ala
                645                 650                 655

Cys Ser Leu Met Leu Thr Gln Phe Val Ser Ser Gln Ala Leu Ala Glu
            660                 665                 670

Leu Ser Thr Ala Met His Gln Val Trp Val Lys Phe Asp Ile Arg Gly
        675                 680                 685

His Cys Pro Cys Gln Ala Asp Ala Arg Val Trp Ala Pro Gly Asp Ala
    690                 695                 700

Gly Gln Gln Lys Glu Ser Thr Gln Lys Thr Pro Pro Thr Pro Gln Pro
705                 710                 715                 720

Ser Cys Asn Gly Asp Thr His Arg Thr Lys Ser Ile Lys Glu Glu Thr
                725                 730                 735

Pro Asp Ser Ala Glu Thr Pro Ala Glu Asp Arg Ala Gly Arg Gly Pro
            740                 745                 750

Leu Pro Cys Pro Ser Leu Cys Glu Leu Leu Ala Ser Thr Ala Val Lys
        755                 760                 765

Leu Cys Leu Gly His Glu Arg Ile His Met Ala Phe Ala Pro Val Thr
    770                 775                 780

Pro Ala Leu Pro Ser Asp Asp Arg Ile Thr Asn Ile Leu Asp Ser Ile
785                 790                 795                 800
```

Ile Ala Gln Val Val Glu Arg Lys Ile Gln Glu Lys Ala Leu Gly Pro
805 810 815

Gly Leu Arg Ala Gly Pro Gly Leu Arg Lys Gly Leu Gly Leu Pro Leu
820 825 830

Ser Pro Val Arg Pro Arg Leu Pro Pro Pro Gly Ala Leu Leu Trp Leu
835 840 845

Gln Glu Pro Gln Pro Cys Pro Arg Arg Gly Phe His Leu Phe Gln Glu
850 855 860

His Trp Arg Gln Gly Gln Pro Val Leu Val Ser Gly Ile Gln Arg Thr
865 870 875 880

Leu Gln Gly Asn Leu Trp Gly Thr Glu Ala Leu Gly Ala Leu Gly Gly
885 890 895

Gln Val Gln Ala Leu Ser Pro Leu Gly Pro Pro Gln Pro Ser Ser Leu
900 905 910

Gly Ser Thr Thr Phe Trp Glu Gly Phe Ser Trp Pro Glu Leu Arg Pro
915 920 925

Lys Ser Asp Glu Gly Ser Val Leu Leu Leu His Arg Ala Leu Gly Asp
930 935 940

Glu Asp Thr Ser Arg Val Glu Asn Leu Ala Ala Ser Leu Pro Leu Pro
945 950 955 960

Glu Tyr Cys Ala Leu His Gly Lys Leu Asn Leu Ala Ser Tyr Leu Pro
965 970 975

Pro Gly Leu Ala Leu Arg Pro Leu Glu Pro Gln Leu Trp Ala Ala Tyr
980 985 990

Gly Val Ser Pro His Arg Gly His Leu Gly Thr Lys Asn Leu Cys Val
995 1000 1005

Glu Val Ala Asp Leu Val Ser Ile Leu Val His Ala Asp Thr Pro
1010 1015 1020

Leu Pro Ala Trp His Arg Ala Gln Lys Asp Phe Leu Ser Gly Leu

1025 1030 1035

Asp Gly Glu Gly Leu Trp Ser Pro Gly Ser Gln Val Ser Thr Val
1040 1045 1050

Trp His Val Phe Arg Ala Gln Asp Ala Gln Arg Ile Arg Arg Phe
1055 1060 1065

Leu Gln Met Val Gln Gly Leu Val Ser Thr Val Ser Val Thr Gln
1070 1075 1080

His Phe Leu Ser Pro Glu Thr Ser Ala Leu Ser Ala Gln Leu Cys
1085 1090 1095

His Gln Gly Pro Ser Leu Pro Pro Asp Cys His Leu Leu Tyr Ala
1100 1105 1110

Gln Met Asp Trp Ala Val Phe Gln Ala Val Lys Val Ala Val Gly
1115 1120 1125

Thr Leu Gln Glu Ala Lys
1130

<210> 143
<211> 142
<212> PRT
<213> Human

<400> 143

Met Val Leu Ser Pro Ala Asp Lys Thr Asn Val Lys Ala Ala Trp Gly
1 5 10 15

Lys Val Gly Ala His Ala Gly Glu Tyr Gly Ala Glu Ala Leu Glu Arg
20 25 30

Met Phe Leu Ser Phe Pro Thr Thr Lys Thr Tyr Phe Pro His Phe Asp
35 40 45

Leu Ser His Gly Ser Ala Gln Val Lys Gly His Gly Lys Lys Val Ala
50 55 60

Asp Ala Leu Thr Asn Ala Val Ala His Val Asp Asp Met Pro Asn Ala
65 70 75 80

Leu Ser Ala Leu Ser Asp Leu His Ala His Lys Leu Arg Val Asp Pro

85 90 95

Val Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala
100 105 110

His Leu Pro Ala Glu Phe Thr Pro Ala Val His Ala Ser Leu Asp Lys
115 120 125

Phe Leu Ala Ser Val Ser Thr Val Leu Thr Ser Lys Tyr Arg
130 135 140

<210> 144
<211> 543
<212> PRT
<213> Human

<400> 144

Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu Leu
1 5 10 15

Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro
20 25 30

Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35 40 45

Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50 55 60

Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65 70 75 80

Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85 90 95

Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
100 105 110

Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
115 120 125

Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
130 135 140

Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe

145 150 155 160

Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
165 170 175

Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
180 185 190

Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
195 200 205

Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
210 215 220

Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
225 230 235 240

Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
245 250 255

Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
260 265 270

Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
275 280 285

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
290 295 300

Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
305 310 315 320

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
325 330 335

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
340 345 350

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
355 360 365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
370 375 380

```
Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
385                 390                 395                 400

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
                405                 410                 415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
            420                 425                 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
        435                 440                 445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
    450                 455                 460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465                 470                 475                 480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
                485                 490                 495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
            500                 505                 510

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
        515                 520                 525

Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
    530                 535                 540
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<210> 145
<211> 203
<212> PRT
<213> Human

<400> 145

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Cys Ser Val Pro Phe Leu Pro Leu Ala Val Pro Val Arg Ala Val His
1               5                   10                  15

Arg Leu Leu Glu His Arg His His Ser Val Thr Trp Pro Ala Thr Glu
            20                  25                  30

Leu Pro Ile Thr Gln Leu Thr Ser Ser Ile Val Arg Arg Val Asn Glu
        35                  40                  45
```

Ala Ser Gly Leu Tyr Gln Met Phe Gly Val Leu Ala Asp Val Ile Leu
50 55 60

Leu Lys Glu Thr Gly Gly Glu Val Pro Pro Cys Thr Leu Ala Pro Ala
65 70 75 80

Ser Ala His Gly His Pro Ser His Arg Gly Arg Leu Leu Asn Arg Leu
85 90 95

Asp Cys Pro Asp Arg Ala His Pro Thr Ser Glu Ala Leu Pro Gly Glu
100 105 110

Leu Phe Gly His Arg Phe Ala Lys Leu Leu Cys Arg Val Leu Leu Pro
115 120 125

Val Arg Pro His Ala Pro Glu Val Ala Thr Leu Leu Pro Ala Gly Val
130 135 140

Pro Glu Asp Ala Gly Thr Arg Glu Tyr Arg Glu Pro Leu Ala Ala Gln
145 150 155 160

Ser Gly Glu Gln Ala Pro Ala Gly Leu Cys Pro His Arg Gln Ala Pro
165 170 175

Gly Gly Gln Gln Pro Ala Ala Trp Arg Pro Arg Ala Thr Arg Phe Pro
180 185 190

Pro Gly Ser Arg Ala Ser Gly Ser Val Arg Arg
195 200

<210> 146
<211> 414
<212> PRT
<213> Human

<400> 146

Met Lys Ala Gln Thr Ala Leu Ser Phe Phe Leu Ile Leu Ile Thr Ser
1 5 10 15

Leu Ser Gly Ser Gln Gly Ile Phe Pro Leu Ala Phe Phe Ile Tyr Val
20 25 30

Pro Met Asn Glu Gln Ile Val Ile Gly Arg Leu Asp Glu Asp Ile Ile
35 40 45

Leu Pro Ser Ser Phe Glu Arg Gly Ser Glu Val Val Ile His Trp Lys
50 55 60

Tyr Gln Asp Ser Tyr Lys Val His Ser Tyr Tyr Lys Gly Ser Asp His
65 70 75 80

Leu Glu Ser Gln Asp Pro Arg Tyr Ala Asn Arg Thr Ser Leu Phe Tyr
85 90 95

Asn Glu Ile Gln Asn Gly Asn Ala Ser Leu Phe Phe Arg Arg Val Ser
100 105 110

Leu Leu Asp Glu Gly Ile Tyr Thr Cys Tyr Val Gly Thr Ala Ile Gln
115 120 125

Val Ile Thr Asn Lys Val Val Leu Lys Val Gly Val Phe Leu Thr Pro
130 135 140

Val Met Lys Tyr Glu Lys Arg Asn Thr Asn Ser Phe Leu Ile Cys Ser
145 150 155 160

Val Leu Ser Val Tyr Pro Arg Pro Ile Ile Thr Trp Lys Met Asp Asn
165 170 175

Thr Pro Ile Ser Glu Asn Asn Met Glu Glu Thr Gly Ser Leu Asp Ser
180 185 190

Phe Ser Ile Asn Ser Pro Leu Asn Ile Thr Gly Ser Asn Ser Ser Tyr
195 200 205

Glu Cys Thr Ile Glu Asn Ser Leu Leu Lys Gln Thr Trp Thr Gly Arg
210 215 220

Trp Thr Met Lys Asp Gly Leu His Lys Met Gln Ser Glu His Val Ser
225 230 235 240

Leu Ser Cys Gln Pro Val Asn Asp Tyr Phe Ser Pro Asn Gln Asp Phe
245 250 255

Lys Val Thr Trp Ser Arg Met Lys Ser Gly Thr Phe Ser Val Leu Ala
260 265 270

Tyr Tyr Leu Ser Ser Ser Gln Asn Thr Ile Ile Asn Glu Ser Arg Phe
275 280 285

Ser Trp Asn Lys Glu Leu Ile Asn Gln Ser Asp Phe Ser Met Asn Leu
    290   295   300

Met Asp Leu Asn Leu Ser Asp Ser Gly Glu Tyr Leu Cys Asn Ile Ser
305   310   315   320

Ser Asp Glu Tyr Thr Leu Leu Thr Ile His Thr Val His Val Glu Pro
                325   330   335

Ser Gln Glu Thr Ala Ser His Asn Lys Gly Leu Trp Ile Leu Val Pro
            340   345   350

Ser Ala Ile Leu Ala Ala Phe Leu Leu Ile Trp Ser Val Lys Cys Cys
        355   360   365

Arg Ala Gln Leu Glu Ala Arg Arg Ser Arg His Pro Ala Asp Gly Ala
    370   375   380

Gln Gln Glu Arg Cys Cys Val Pro Pro Gly Glu Arg Cys Pro Ser Ala
385   390   395   400

Pro Asp Asn Gly Glu Glu Asn Val Pro Leu Ser Gly Lys Val
                405   410

<210> 147
<211> 545
<212> PRT
<213> Human

<400> 147

Met Val Asp Ala Ala Glu Asn Leu Cys Pro Asn Val Met Lys Lys Ala
1   5   10   15

His Ile Arg Gln Asp Leu Ile His Ala Ser Thr Glu Lys Ile Ser Ile
            20   25   30

Pro Arg Thr Phe Val Lys Asn Val Leu Leu Glu Gln Ser Gly Ile Asp
        35   40   45

Ile Leu Asn Lys Ile Ser Glu Val Lys Leu Thr Val Ala Ser Phe Leu
    50   55   60

Ser Asp Arg Ile Val Asp Glu Ile Leu Asp Ala Leu Ser His Cys His
65   70   75   80

His Lys Leu Ala Asp His Phe Ser Arg Arg Gly Lys Thr Leu Pro Gln
85 90 95

Gln Glu Ser Leu Glu Ile Glu Leu Ala Glu Glu Arg Pro Val Lys Arg
100 105 110

Ser Ile Ile Thr Val Glu Glu Leu Thr Glu Ile Glu Arg Leu Glu Asp
115 120 125

Leu Asp Thr Cys Met Met Thr Pro Lys Ser Lys Arg Lys Ser Ile His
130 135 140

Ser Arg Met Leu Arg Pro Val Ser Arg Ala Phe Glu Met Glu Phe Asp
145 150 155 160

Leu Asp Lys Ala Leu Glu Glu Val Pro Ile His Ile Glu Asp Pro Pro
165 170 175

Phe Pro Ser Leu Arg Gln Glu Lys Arg Ser Ser Gly Phe Ile Ser Glu
180 185 190

Leu Pro Ser Glu Glu Gly Lys Lys Leu Glu His Phe Thr Lys Leu Arg
195 200 205

Pro Lys Arg Asn Lys Lys Gln Gln Pro Thr Gln Ala Ala Val Cys Ala
210 215 220

Ala Asn Ile Val Ser Gln Asp Gly Glu Gln Asn Gly Leu Met Gly Arg
225 230 235 240

Val Asp Glu Gly Val Asp Glu Phe Phe Thr Lys Lys Val Thr Lys Met
245 250 255

Asp Ser Lys Lys Trp Ser Thr Arg Gly Ser Glu Ser His Glu Leu Asn
260 265 270

Glu Gly Gly Asp Glu Lys Lys Lys Arg Asp Ser Arg Lys Ser Ser Gly
275 280 285

Phe Leu Asn Leu Ile Lys Ser Arg Ser Lys Ser Glu Arg Pro Pro Thr
290 295 300

Ile Leu Met Thr Glu Glu Pro Ser Ser Pro Lys Gly Ala Val Arg Ser
305 310 315 320

Pro Pro Val Asp Cys Pro Arg Lys Asp Thr Lys Ala Ala Glu His Asn
325 330 335

Gly Asn Ser Glu Arg Ile Glu Glu Ile Lys Thr Pro Asp Ser Phe Glu
340 345 350

Glu Ser Gln Gly Glu Glu Ile Gly Lys Val Glu Arg Ser Asp Ser Lys
355 360 365

Ser Ser Pro Gln Ala Gly Arg Arg Tyr Gly Val Gln Val Met Gly Ser
370 375 380

Gly Leu Leu Ala Glu Met Lys Ala Lys Gln Glu Asn Arg Phe Gly Leu
385 390 395 400

Gly Thr Pro Glu Lys Asn Thr Lys Ala Glu Pro Lys Ala Glu Ala Gly
405 410 415

Ser Arg Ser Arg Ser Ser Ser Ser Thr Pro Thr Ser Pro Lys Pro Leu
420 425 430

Leu Gln Ser Pro Lys Pro Ser Leu Ala Ala Arg Pro Val Ile Pro Gln
435 440 445

Lys Pro Arg Thr Ala Ser Arg Pro Asp Asp Ile Pro Asp Ser Pro Ser
450 455 460

Ser Pro Lys Val Ala Leu Leu Pro Pro Val Leu Lys Lys Val Pro Ser
465 470 475 480

Asp Lys Glu Arg Asp Gly Gln Ser Ser Pro Gln Pro Ser Pro Arg Thr
485 490 495

Phe Ser Gln Glu Val Ser Arg Arg Ser Trp Gly Gln Gln Ala Gln Glu
500 505 510

Tyr Gln Glu Gln Lys Gln Arg Ser Ser Ser Lys Asp Gly His Gln Gly
515 520 525

Ser Lys Ser Asn Asp Ser Gly Glu Glu Ala Glu Lys Glu Phe Ile Phe
530 535 540

Val

545

<210> 148
<211> 315
<212> PRT
<213> Human

<400> 148

Met Pro Leu Lys Leu Arg Gly Lys Lys Lys Ala Lys Ser Lys Glu Thr
1 5 10 15

Ala Gly Leu Val Glu Gly Glu Pro Thr Gly Ala Gly Gly Gly Ser Leu
20 25 30

Ser Ala Ser Arg Ala Pro Ala Arg Arg Leu Val Phe His Ala Gln Leu
35 40 45

Ala His Gly Ser Ala Thr Gly Arg Val Glu Gly Phe Ser Ser Ile Gln
50 55 60

Glu Leu Tyr Ala Gln Ile Ala Gly Ala Phe Glu Ile Ser Pro Ser Glu
65 70 75 80

Ile Leu Tyr Cys Thr Leu Asn Thr Pro Lys Ile Asp Met Glu Arg Leu
85 90 95

Leu Gly Gly Gln Leu Gly Leu Glu Asp Phe Ile Phe Ala His Val Lys
100 105 110

Gly Ile Glu Lys Glu Val Asn Val Tyr Lys Ser Glu Asp Ser Leu Gly
115 120 125

Leu Thr Ile Thr Asp Asn Gly Val Gly Tyr Ala Phe Ile Lys Arg Ile
130 135 140

Lys Asp Gly Gly Val Ile Asp Ser Val Lys Thr Ile Cys Val Gly Asp
145 150 155 160

His Ile Glu Ser Ile Asn Gly Glu Asn Ile Val Gly Trp Arg His Tyr
165 170 175

Asp Val Ala Lys Lys Leu Lys Glu Leu Lys Lys Glu Glu Leu Phe Thr
180 185 190

Met Lys Leu Ile Glu Pro Lys Lys Ala Phe Glu Ile Glu Leu Arg Ser

195 200 205

Lys Ala Gly Lys Ser Ser Gly Glu Lys Ile Gly Cys Gly Arg Ala Thr
210 215 220

Leu Arg Leu Arg Ser Lys Gly Pro Ala Thr Val Glu Glu Met Pro Ser
225 230 235 240

Glu Thr Lys Ala Lys Ala Ile Glu Lys Ile Asp Asp Val Leu Glu Leu
245 250 255

Tyr Met Gly Ile Arg Asp Ile Asp Leu Ala Thr Thr Met Phe Glu Ala
260 265 270

Gly Lys Asp Lys Val Asn Pro Asp Glu Phe Ala Val Ala Leu Asp Glu
275 280 285

Thr Leu Gly Asp Phe Ala Phe Pro Asp Glu Phe Val Phe Asp Val Trp
290 295 300

Gly Val Ile Gly Asp Ala Lys Arg Arg Gly Leu
305 310 315

<210> 149
<211> 486
<212> PRT
<213> Human

<400> 149

Met Pro Arg Pro Ala Pro Ala Arg Arg Leu Pro Gly Leu Leu Leu Leu
1 5 10 15

Leu Trp Pro Leu Leu Leu Leu Pro Ser Ala Ala Pro Asp Pro Val Ala
20 25 30

Arg Pro Gly Phe Arg Arg Leu Glu Thr Arg Gly Pro Gly Gly Ser Pro
35 40 45

Gly Arg Arg Pro Ser Pro Ala Ala Pro Asp Gly Ala Pro Ala Ser Gly
50 55 60

Thr Ser Glu Pro Gly Arg Ala Arg Gly Ala Gly Val Cys Lys Ser Arg
65 70 75 80

Pro Leu Asp Leu Val Phe Ile Ile Asp Ser Ser Arg Ser Val Arg Pro

85 90 95

Leu Glu Phe Thr Lys Val Lys Thr Phe Val Ser Arg Ile Ile Asp Thr
100 105 110

Leu Asp Ile Gly Pro Ala Asp Thr Arg Val Ala Val Val Asn Tyr Ala
115 120 125

Ser Thr Val Lys Ile Glu Phe Gln Leu Gln Ala Tyr Thr Asp Lys Gln
130 135 140

Ser Leu Lys Gln Ala Val Gly Arg Ile Thr Pro Leu Ser Thr Gly Thr
145 150 155 160

Met Ser Gly Leu Ala Ile Gln Thr Ala Met Asp Glu Ala Phe Thr Val
165 170 175

Glu Ala Gly Ala Arg Glu Pro Ser Ser Asn Ile Pro Lys Val Ala Ile
180 185 190

Ile Val Thr Asp Gly Arg Pro Gln Asp Gln Val Asn Glu Val Ala Ala
195 200 205

Arg Ala Gln Ala Ser Gly Ile Glu Leu Tyr Ala Val Gly Val Asp Arg
210 215 220

Ala Asp Met Ala Ser Leu Lys Met Met Ala Ser Glu Pro Leu Glu Glu
225 230 235 240

His Val Phe Tyr Val Glu Thr Tyr Gly Val Ile Glu Lys Leu Ser Ser
245 250 255

Arg Phe Gln Glu Thr Phe Cys Ala Leu Asp Pro Cys Val Leu Gly Thr
260 265 270

His Gln Cys Gln His Val Cys Ile Ser Asp Gly Glu Gly Lys His His
275 280 285

Cys Glu Cys Ser Gln Gly Tyr Thr Leu Asn Ala Asp Lys Lys Thr Cys
290 295 300

Ser Ala Leu Asp Arg Cys Ala Leu Asn Thr His Gly Cys Glu His Ile
305 310 315 320

Cys Val Asn Asp Arg Ser Gly Ser Tyr His Cys Glu Cys Tyr Glu Gly
325 330 335

Tyr Thr Leu Asn Glu Asp Arg Lys Thr Cys Ser Ala Gln Asp Lys Cys
340 345 350

Ala Leu Gly Thr His Gly Cys Gln His Ile Cys Val Asn Asp Arg Thr
355 360 365

Gly Ser His His Cys Glu Cys Tyr Glu Gly Tyr Thr Leu Asn Ala Asp
370 375 380

Lys Lys Thr Cys Ser Val Arg Asp Lys Cys Ala Leu Gly Ser His Gly
385 390 395 400

Cys Gln His Ile Cys Val Ser Asp Gly Ala Ala Ser Tyr His Cys Asp
405 410 415

Cys Tyr Pro Gly Tyr Thr Leu Asn Glu Asp Lys Lys Thr Cys Ser Ala
420 425 430

Thr Glu Glu Ala Arg Arg Leu Val Ser Thr Glu Asp Ala Cys Gly Cys
435 440 445

Glu Ala Thr Leu Ala Phe Gln Asp Lys Val Ser Ser Tyr Leu Gln Arg
450 455 460

Leu Asn Thr Lys Leu Asp Asp Ile Leu Glu Lys Leu Lys Ile Asn Glu
465 470 475 480

Tyr Gly Gln Ile His Arg
485

<210> 150
<211> 668
<212> PRT
<213> Human

<400> 150

Met Ala Ala Asn Met Tyr Arg Val Gly Asp Tyr Val Tyr Phe Glu Asn
1 5 10 15

Ser Ser Ser Asn Pro Tyr Leu Val Arg Arg Ile Glu Glu Leu Asn Lys
20 25 30

Thr Ala Asn Gly Asn Val Glu Ala Lys Val Val Cys Leu Phe Arg Arg
35 40 45

Arg Asp Ile Ser Ser Ser Leu Asn Ser Leu Ala Asp Ser Asn Ala Arg
50 55 60

Glu Phe Glu Glu Glu Ser Lys Gln Pro Gly Val Ser Glu Gln Gln Arg
65 70 75 80

His Gln Leu Lys His Arg Glu Leu Phe Leu Ser Arg Gln Phe Glu Ser
85 90 95

Leu Pro Ala Thr His Ile Arg Gly Lys Cys Ser Val Thr Leu Leu Asn
100 105 110

Glu Thr Asp Ile Leu Ser Gln Tyr Leu Glu Lys Glu Asp Cys Phe Phe
115 120 125

Tyr Ser Leu Val Phe Asp Pro Val Gln Lys Thr Leu Leu Ala Asp Gln
130 135 140

Gly Glu Ile Arg Val Gly Cys Lys Tyr Gln Ala Glu Ile Pro Asp Arg
145 150 155 160

Leu Val Glu Gly Glu Ser Asp Asn Arg Asn Gln Gln Lys Met Glu Met
165 170 175

Lys Val Trp Asp Pro Asp Asn Pro Leu Thr Asp Arg Gln Ile Asp Gln
180 185 190

Phe Leu Val Val Ala Arg Ala Val Gly Thr Phe Ala Arg Ala Leu Asp
195 200 205

Cys Ser Ser Ser Ile Arg Gln Pro Ser Leu His Met Ser Ala Ala Ala
210 215 220

Ala Ser Arg Asp Ile Thr Leu Phe His Ala Met Asp Thr Leu Gln Arg
225 230 235 240

Asn Gly Tyr Asp Leu Ala Lys Ala Met Ser Thr Leu Val Pro Gln Gly
245 250 255

Gly Pro Val Leu Cys Arg Asp Glu Met Glu Glu Trp Ser Ala Ser Glu
260 265 270

Ala Met Leu Phe Glu Glu Ala Leu Glu Lys Tyr Gly Lys Asp Phe Asn
275 280 285

Asp Ile Arg Gln Asp Phe Leu Pro Trp Lys Ser Leu Ala Ser Ile Val
290 295 300

Gln Phe Tyr Tyr Met Trp Lys Thr Thr Asp Arg Tyr Ile Gln Gln Lys
305 310 315 320

Arg Leu Lys Ala Ala Glu Ala Asp Ser Lys Leu Lys Gln Val Tyr Ile
325 330 335

Pro Thr Tyr Thr Lys Pro Asn Pro Asn Gln Ile Ile Ser Val Gly Ser
340 345 350

Lys Pro Gly Met Asn Gly Ala Gly Phe Gln Lys Gly Leu Thr Cys Glu
355 360 365

Ser Cys His Thr Thr Gln Ser Ala Gln Trp Tyr Ala Trp Gly Pro Pro
370 375 380

Asn Met Gln Cys Arg Leu Cys Ala Ser Cys Trp Ile Tyr Trp Lys Lys
385 390 395 400

Tyr Gly Gly Leu Lys Thr Pro Thr Gln Leu Glu Gly Ala Thr Arg Gly
405 410 415

Thr Thr Glu Pro His Ser Arg Gly His Leu Ser Arg Pro Glu Ala Gln
420 425 430

Ser Leu Ser Pro Tyr Thr Thr Ser Ala Asn Arg Ala Lys Leu Leu Ala
435 440 445

Lys Asn Arg Gln Thr Phe Leu Leu Gln Thr Thr Lys Leu Thr Arg Leu
450 455 460

Ala Arg Arg Met Cys Arg Asp Leu Leu Gln Pro Arg Arg Ala Ala Arg
465 470 475 480

Arg Pro Tyr Ala Pro Ile Asn Ala Asn Ala Ile Lys Ala Glu Cys Ser
485 490 495

Ile Arg Leu Pro Lys Ala Ala Lys Thr Pro Leu Lys Ile His Pro Leu
500 505 510

Val Arg Leu Pro Leu Ala Thr Ile Val Lys Asp Leu Val Ala Gln Ala
515 520 525

Pro Leu Lys Pro Lys Thr Pro Arg Gly Thr Lys Thr Pro Ile Asn Arg
530 535 540

Asn Gln Leu Ser Gln Asn Arg Gly Leu Gly Gly Ile Met Val Lys Arg
545 550 555 560

Ala Tyr Glu Thr Met Ala Gly Ala Gly Val Pro Phe Ser Ala Asn Gly
565 570 575

Arg Pro Leu Ala Ser Gly Ile Arg Ser Ser Ser Gln Pro Ala Ala Lys
580 585 590

Arg Gln Lys Leu Asn Pro Ala Asp Ala Pro Asn Pro Val Val Phe Val
595 600 605

Ala Thr Lys Asp Thr Arg Ala Leu Arg Lys Ala Leu Thr His Leu Glu
610 615 620

Met Arg Arg Ala Ala Arg Arg Pro Asn Leu Pro Leu Lys Val Lys Pro
625 630 635 640

Thr Leu Ile Ala Val Arg Pro Pro Val Pro Leu Pro Ala Pro Ser His
645 650 655

Pro Ala Ser Thr Asn Glu Pro Ile Val Leu Glu Asp
660 665

<210> 151
<211> 5179
<212> PRT
<213> Human

<400> 151

Met Gly Leu Pro Leu Ala Arg Leu Ala Ala Val Cys Leu Ala Leu Ser
1 5 10 15

Leu Ala Gly Gly Ser Glu Leu Gln Thr Glu Gly Arg Thr Arg Tyr His
20 25 30

Gly Arg Asn Val Cys Ser Thr Trp Gly Asn Phe His Tyr Lys Thr Phe
35 40 45

Asp Gly Asp Val Phe Arg Phe Pro Gly Leu Cys Asp Tyr Asn Phe Ala
    50   55   60

Ser Asp Cys Arg Gly Ser Tyr Lys Glu Phe Ala Val His Leu Lys Arg
65   70   75   80

Gly Pro Gly Gln Ala Glu Ala Pro Ala Gly Val Glu Ser Ile Leu Leu
                85   90   95

Thr Ile Lys Asp Asp Thr Ile Tyr Leu Thr Arg His Leu Ala Val Leu
            100   105   110

Asn Gly Ala Val Val Ser Thr Pro His Tyr Ser Pro Gly Leu Leu Ile
        115   120   125

Glu Lys Ser Asp Ala Tyr Thr Lys Val Tyr Ser Arg Ala Gly Leu Thr
    130   135   140

Leu Met Trp Asn Arg Glu Asp Ala Leu Met Leu Glu Leu Asp Thr Lys
145   150   155   160

Phe Arg Asn His Thr Cys Gly Leu Cys Gly Asp Tyr Asn Gly Leu Gln
                165   170   175

Ser Tyr Ser Glu Phe Leu Ser Asp Gly Val Leu Phe Ser Pro Leu Glu
            180   185   190

Phe Gly Asn Met Gln Lys Ile Asn Gln Pro Asp Val Val Cys Glu Asp
        195   200   205

Pro Glu Glu Glu Val Ala Pro Ala Ser Cys Ser Glu His Arg Ala Glu
    210   215   220

Cys Glu Arg Leu Leu Thr Ala Glu Ala Phe Ala Asp Cys Gln Asp Leu
225   230   235   240

Val Pro Leu Glu Pro Tyr Leu Arg Ala Cys Gln Gln Asp Arg Cys Arg
                245   250   255

Cys Pro Gly Gly Asp Thr Cys Val Cys Ser Thr Val Ala Glu Phe Ser
            260   265   270

Arg Gln Cys Ser His Ala Gly Gly Arg Pro Gly Asn Trp Arg Thr Ala

275 280 285

Thr Leu Cys Pro Lys Thr Cys Pro Gly Asn Leu Val Tyr Leu Glu Ser
290 295 300

Gly Ser Pro Cys Met Asp Thr Cys Ser His Leu Glu Val Ser Ser Leu
305 310 315 320

Cys Glu Glu His Arg Met Asp Gly Cys Phe Cys Pro Glu Gly Thr Val
325 330 335

Tyr Asp Asp Ile Gly Asp Ser Gly Cys Val Pro Val Ser Gln Cys His
340 345 350

Cys Arg Leu His Gly His Leu Tyr Thr Pro Gly Gln Glu Ile Thr Asn
355 360 365

Asp Cys Glu Gln Cys Val Cys Asn Ala Gly Arg Trp Val Cys Lys Asp
370 375 380

Leu Pro Cys Pro Gly Thr Cys Ala Leu Glu Gly Gly Ser His Ile Thr
385 390 395 400

Thr Phe Asp Gly Lys Thr Tyr Thr Phe His Gly Asp Cys Tyr Tyr Val
405 410 415

Leu Ala Lys Gly Asp His Asn Asp Ser Tyr Ala Leu Leu Gly Glu Leu
420 425 430

Ala Pro Cys Gly Ser Thr Asp Lys Gln Thr Cys Leu Lys Thr Val Val
435 440 445

Leu Leu Ala Asp Lys Lys Lys Asn Ala Val Val Phe Lys Ser Asp Gly
450 455 460

Ser Val Leu Leu Asn Gln Leu Gln Val Asn Leu Pro His Val Thr Ala
465 470 475 480

Ser Phe Ser Val Phe Arg Pro Ser Ser Tyr His Ile Met Val Ser Met
485 490 495

Ala Ile Gly Val Arg Leu Gln Val Gln Leu Ala Pro Val Met Gln Leu
500 505 510

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Phe Val Thr Leu Asp Gln Ala Ser Gln Gly Gln Val Gln Gly Leu Cys
        515                 520                 525

Gly Asn Phe Asn Gly Leu Glu Gly Asp Asp Phe Lys Thr Ala Ser Gly
    530                 535                 540

Leu Val Glu Ala Thr Gly Ala Gly Phe Ala Asn Thr Trp Lys Ala Gln
545                 550                 555                 560

Ser Thr Cys His Asp Lys Leu Asp Trp Leu Asp Asp Pro Cys Ser Leu
                565                 570                 575

Asn Ile Glu Ser Ala Asn Tyr Ala Glu His Trp Cys Ser Leu Leu Lys
            580                 585                 590

Lys Thr Glu Thr Pro Phe Gly Arg Cys His Ser Ala Val Asp Pro Ala
        595                 600                 605

Glu Tyr Tyr Lys Arg Cys Lys Tyr Asp Thr Cys Asn Cys Gln Asn Asn
    610                 615                 620

Glu Asp Cys Leu Cys Ala Ala Leu Ser Ser Tyr Ala Arg Ala Cys Thr
625                 630                 635                 640

Ala Lys Gly Val Met Leu Trp Gly Trp Arg Glu His Val Cys Asn Lys
                645                 650                 655

Asp Val Gly Ser Cys Pro Asn Ser Gln Val Phe Leu Tyr Asn Leu Thr
            660                 665                 670

Thr Cys Gln Gln Thr Cys Arg Ser Leu Ser Glu Ala Asp Ser His Cys
        675                 680                 685

Leu Glu Gly Phe Ala Pro Val Asp Gly Cys Gly Cys Pro Asp His Thr
    690                 695                 700

Phe Leu Asp Glu Lys Gly Arg Cys Val Pro Leu Ala Lys Cys Ser Cys
705                 710                 715                 720

Tyr His Arg Gly Leu Tyr Leu Glu Ala Gly Asp Val Val Val Arg Gln
                725                 730                 735

Glu Glu Arg Cys Val Cys Arg Asp Gly Arg Leu His Cys Arg Gln Ile
            740                 745                 750
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Arg Leu Ile Gly Gln Ser Cys Thr Ala Pro Lys Ile His Met Asp Cys
755 760 765

Ser Asn Leu Thr Ala Leu Ala Thr Ser Lys Pro Arg Ala Leu Ser Cys
770 775 780

Gln Thr Leu Ala Ala Gly Tyr Tyr His Thr Glu Cys Val Ser Gly Cys
785 790 795 800

Val Cys Pro Asp Gly Leu Met Asp Asp Gly Arg Gly Gly Cys Val Val
805 810 815

Glu Lys Glu Cys Pro Cys Val His Asn Asn Asp Leu Tyr Ser Ser Gly
820 825 830

Ala Lys Ile Lys Val Asp Cys Asn Thr Cys Thr Cys Lys Arg Gly Arg
835 840 845

Trp Val Cys Thr Gln Ala Val Cys His Gly Thr Cys Ser Ile Tyr Gly
850 855 860

Ser Gly His Tyr Ile Thr Phe Asp Gly Lys Tyr Tyr Asp Phe Asp Gly
865 870 875 880

His Cys Ser Tyr Val Ala Val Gln Asp Tyr Cys Gly Gln Asn Ser Ser
885 890 895

Leu Gly Ser Phe Ser Ile Ile Thr Glu Asn Val Pro Cys Gly Thr Thr
900 905 910

Gly Val Thr Cys Ser Lys Ala Ile Lys Ile Phe Met Gly Arg Thr Glu
915 920 925

Leu Lys Leu Glu Asp Lys His Arg Val Val Ile Gln Arg Asp Glu Gly
930 935 940

His His Val Ala Tyr Thr Thr Arg Glu Val Gly Gln Tyr Leu Val Val
945 950 955 960

Glu Ser Ser Thr Gly Ile Ile Val Ile Trp Asp Lys Arg Thr Thr Val
965 970 975

Phe Ile Lys Leu Ala Pro Ser Tyr Lys Gly Thr Val Cys Gly Leu Cys
980 985 990

Gly Asn Phe Asp His Arg Ser Asn Asn Asp Phe Thr Thr Arg Asp His
995 1000 1005

Met Val Val Ser Ser Glu Leu Asp Phe Gly Asn Ser Trp Lys Glu
1010 1015 1020

Ala Pro Thr Cys Pro Asp Val Ser Thr Asn Pro Glu Pro Cys Ser
1025 1030 1035

Leu Asn Pro His Arg Arg Ser Trp Ala Glu Lys Gln Cys Ser Ile
1040 1045 1050

Leu Lys Ser Ser Val Phe Ser Ile Cys His Ser Lys Val Asp Pro
1055 1060 1065

Lys Pro Phe Tyr Glu Ala Cys Val His Asp Ser Cys Ser Cys Asp
1070 1075 1080

Thr Gly Gly Asp Cys Glu Cys Phe Cys Ser Ala Val Ala Ser Tyr
1085 1090 1095

Ala Gln Glu Cys Thr Lys Glu Gly Ala Cys Val Phe Trp Arg Thr
1100 1105 1110

Pro Asp Leu Cys Pro Ile Phe Cys Asp Tyr Tyr Asn Pro Pro His
1115 1120 1125

Glu Cys Glu Trp His Tyr Glu Pro Cys Gly Asn Arg Ser Phe Glu
1130 1135 1140

Thr Cys Arg Thr Ile Asn Gly Ile His Ser Asn Ile Ser Val Ser
1145 1150 1155

Tyr Leu Glu Gly Cys Tyr Pro Arg Cys Pro Lys Asp Arg Pro Ile
1160 1165 1170

Tyr Glu Glu Asp Leu Lys Lys Cys Val Thr Ala Asp Lys Cys Gly
1175 1180 1185

Cys Tyr Val Glu Asp Thr His Tyr Pro Pro Gly Ala Ser Val Pro
1190 1195 1200

Thr Glu Glu Thr Cys Lys Ser Cys Val Cys Thr Asn Ser Ser Gln

1205 1210 1215

Val Val Cys Arg Pro Glu Glu Gly Lys Ile Leu Asn Gln Thr Gln
1220 1225 1230

Asp Gly Ala Phe Cys Tyr Trp Glu Ile Cys Gly Pro Asn Gly Thr
1235 1240 1245

Val Glu Lys His Phe Asn Ile Cys Ser Ile Thr Thr Arg Pro Ser
1250 1255 1260

Thr Leu Thr Thr Phe Thr Thr Ile Thr Leu Pro Thr Thr Pro Thr
1265 1270 1275

Ser Phe Thr Thr Thr Thr Thr Thr Thr Thr Pro Thr Ser Ser Thr
1280 1285 1290

Val Leu Ser Thr Thr Pro Lys Leu Cys Cys Leu Trp Ser Asp Trp
1295 1300 1305

Ile Asn Glu Asp His Pro Ser Ser Gly Ser Asp Asp Gly Asp Arg
1310 1315 1320

Glu Pro Phe Asp Gly Val Cys Gly Ala Pro Glu Asp Ile Glu Cys
1325 1330 1335

Arg Ser Val Lys Asp Pro His Leu Ser Leu Glu Gln His Gly Gln
1340 1345 1350

Lys Val Gln Cys Asp Val Ser Val Gly Phe Ile Cys Lys Asn Glu
1355 1360 1365

Asp Gln Phe Gly Asn Gly Pro Phe Gly Leu Cys Tyr Asp Tyr Lys
1370 1375 1380

Ile Arg Val Asn Cys Cys Trp Pro Met Asp Lys Cys Ile Thr Thr
1385 1390 1395

Pro Ser Pro Pro Thr Thr Thr Pro Ser Pro Pro Pro Thr Thr Thr
1400 1405 1410

Thr Thr Leu Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr
1415 1420 1425

Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro Ile Thr
1430 1435 1440

Thr Thr Thr Thr Pro Leu Pro Thr Thr Thr Pro Ser Pro Pro Ile
1445 1450 1455

Ser Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro
1460 1465 1470

Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr
1475 1480 1485

Thr Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro
1490 1495 1500

Met Thr Thr Pro Ile Thr Pro Pro Ala Ser Thr Thr Thr Leu Pro
1505 1510 1515

Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Thr Thr Thr Pro
1520 1525 1530

Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Pro Ile Thr
1535 1540 1545

Pro Pro Thr Ser Thr Thr Thr Leu Pro Pro Thr Thr Thr Pro Ser
1550 1555 1560

Pro Pro Pro Thr Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro
1565 1570 1575

Ser Pro Pro Thr Thr Thr Thr Pro Ser Pro Pro Thr Ile Thr Thr
1580 1585 1590

Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr
1595 1600 1605

Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr
1610 1615 1620

Thr Pro Ile Thr Pro Pro Thr Ser Thr Thr Thr Leu Pro Pro Thr
1625 1630 1635

Thr Thr Pro Ser Pro Pro Pro Thr Thr Thr Thr Thr Pro Pro Pro
1640 1645 1650

Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Thr Pro Ser Pro Pro
1655 1660 1665

Ile Thr Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Ser
1670 1675 1680

Pro Ile Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Met Thr Thr
1685 1690 1695

Pro Ser Pro Thr Thr Thr Pro Ser Ser Pro Ile Thr Thr Thr Thr
1700 1705 1710

Thr Pro Ser Ser Thr Thr Thr Pro Ser Pro Pro Pro Thr Thr Met
1715 1720 1725

Thr Thr Pro Ser Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr
1730 1735 1740

Met Thr Thr Leu Pro Pro Thr Thr Thr Ser Ser Pro Leu Thr Thr
1745 1750 1755

Thr Pro Leu Pro Pro Ser Ile Thr Pro Pro Thr Phe Ser Pro Phe
1760 1765 1770

Ser Thr Thr Thr Pro Thr Thr Pro Cys Val Pro Leu Cys Asn Trp
1775 1780 1785

Thr Gly Trp Leu Asp Ser Gly Lys Pro Asn Phe His Lys Pro Gly
1790 1795 1800

Gly Asp Thr Glu Leu Ile Gly Asp Val Cys Gly Pro Gly Trp Ala
1805 1810 1815

Ala Asn Ile Ser Cys Arg Ala Thr Met Tyr Pro Asp Val Pro Ile
1820 1825 1830

Gly Gln Leu Gly Gln Thr Val Val Cys Asp Val Ser Val Gly Leu
1835 1840 1845

Ile Cys Lys Asn Glu Asp Gln Lys Pro Gly Gly Val Ile Pro Met
1850 1855 1860

Ala Phe Cys Leu Asn Tyr Glu Ile Asn Val Gln Cys Cys Glu Cys
1865 1870 1875

Val Thr Gln Pro Thr Thr Met Thr Thr Thr Thr Thr Glu Asn Pro
1880 1885 1890

Thr Pro Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr
1895 1900 1905

Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro
1910 1915 1920

Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly
1925 1930 1935

Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val
1940 1945 1950

Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr
1955 1960 1965

Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr
1970 1975 1980

Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr
1985 1990 1995

Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr
2000 2005 2010

Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro
2015 2020 2025

Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr
2030 2035 2040

Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr
2045 2050 2055

Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr
2060 2065 2070

Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr
2075 2080 2085

Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro

2090 2095 2100

Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro
2105 2110 2115

Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr
2120 2125 2130

Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr
2135 2140 2145

Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr
2150 2155 2160

Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr
2165 2170 2175

Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln
2180 2185 2190

Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro
2195 2200 2205

Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile
2210 2215 2220

Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr
2225 2230 2235

Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr
2240 2245 2250

Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro
2255 2260 2265

Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly
2270 2275 2280

Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val
2285 2290 2295

Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr
2300 2305 2310

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Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr
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Leu Glu Phe Tyr Asn Trp Ser Cys Pro Ser Thr Pro Ser Pro Thr
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Val Lys Val Glu Cys Glu Pro Pro Pro Met Pro Thr Cys Ser Asn
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Gly Leu Gln Pro Val Arg Val Glu Asp Pro Asp Gly Cys Cys Trp
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His Trp Glu Cys Asp Cys Tyr Cys Thr Gly Trp Gly Asp Pro His
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Tyr Val Thr Phe Asp Gly Leu Tyr Tyr Ser Tyr Gln Gly Asn Cys
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Thr Tyr Val Leu Val Glu Glu Ile Ser Pro Ser Val Asp Asn Phe
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Gly Val Tyr Ile Asp Asn Tyr His Cys Asp Pro Asn Asp Lys Val
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Ser Cys Pro Arg Thr Leu Ile Val Arg His Glu Thr Gln Glu Val
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Leu Ile Lys Thr Val His Met Met Pro Met Gln Val Gln Val Gln
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Val Asn Arg Gln Ala Val Ala Leu Pro Tyr Lys Lys Tyr Gly Leu
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Glu Val Tyr Gln Ser Gly Ile Asn Tyr Val Val Asp Ile Pro Glu
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Leu Gly Val Leu Val Ser Tyr Asn Gly Leu Ser Phe Ser Val Arg
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Leu Pro Tyr His Arg Phe Gly Asn Asn Thr Lys Gly Gln Cys Gly
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Glu Ile Val Ser Asn Cys Glu Ala Ala Ala Asp Gln Trp Leu Val
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Asn Asp Pro Ser Lys Pro His Cys Pro His Ser Ser Ser Thr Thr
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Lys Arg Pro Ala Val Thr Val Pro Gly Gly Gly Lys Thr Thr Pro
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His Lys Asp Cys Thr Pro Ser Pro Leu Cys Gln Leu Ile Lys Asp
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Ser Leu Phe Ala Gln Cys His Ala Leu Val Pro Pro Gln His Tyr
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Tyr Asp Ala Cys Val Phe Asp Ser Cys Phe Met Pro Gly Ser Ser
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Leu Glu Cys Ala Ser Leu Gln Ala Tyr Ala Ala Leu Cys Ala Gln
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Gln Asn Ile Cys Leu Asp Trp Arg Asn His Thr His Gly Ala Cys

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Leu Val Glu Cys Pro Ser His Arg Glu Tyr Gln Ala Cys Gly Pro
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Cys Gln Pro Lys Arg Cys Ser Gln Lys Pro Val Thr His Cys Val
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Val Tyr Ser Ser Lys Cys Gln Asp Cys Val Cys Thr Asp Lys Val
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Glu Asn Thr Pro Ile Ser Ser Phe Ser Thr Ser Ile Val Val Thr Pro
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Glu Thr Pro Thr Thr Gln Ala Pro Pro Val Leu Met Ser Ala Thr Gly
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Ser Ser Thr Ser Thr Leu His Thr Leu Thr Pro Ser Thr Ala Leu Ser
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Thr Leu Gln Thr Thr Pro Ser Ile Pro Ser Leu Gln Thr Ser Leu Thr
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Thr Asn Ala Ile Leu Thr Ser Phe Ser Thr Ile Ile Trp Ser Ser Thr
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Pro Thr Ile Ile Met Ser Ser Ser Pro Ser Ser Ala Ser Ile Thr Pro
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Val Phe Ala Thr Thr Ile His Ser Val Pro Ser Ser Pro Tyr Ile Phe
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Ser Thr Glu Asn Val Gly Ser Ala Ser Ile Thr Ala Phe Pro Ser Leu
        275                 280                 285

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Thr Ala Leu Thr Glu Ile Thr Pro Phe Ser Tyr Ile Ser Leu Pro Ser
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Pro Pro Thr Thr Pro Leu Thr Val Phe Pro Phe Thr Thr Glu Met Val
        355                 360                 365

Thr Cys Pro Ser Ser Ile Ser Met Gln Thr Thr Leu Ala Thr His Met
    370                 375                 380

Asp Thr Ser Ser Met Thr Pro Glu Ser Glu Ser Ser Ile Ile Pro Asn
385                 390                 395                 400

Ala Ser Ser Ser Thr Gly Thr Gly Thr Val Pro Thr Asn Thr Val Phe
                405                 410                 415

Thr Ser Thr Arg Leu Pro Thr Ser Glu Thr Trp Leu Ser Asn Asn Ser
            420                 425                 430

Val Ile Pro Thr Pro Leu Pro Gly Val Ser Thr Ile Pro Leu Thr Met
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Lys Pro Ser Ser Ser Leu Pro Thr Ile Leu Arg Thr Ser Ser Lys Ser
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Gly Phe Ser Gly Asp Arg Cys Gln Leu Gln Thr Arg Cys Gln Asn Gly
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Gly Gln Trp Asp Gly Leu Lys Cys Gln Cys Pro Ser Thr Phe Tyr Gly
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Ser Ser Cys Glu Phe Ala Val Glu Gln Val Asp Leu Asp Val Val Glu
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Thr Glu Val Gly Met Glu Val Ser Val Asp Gln Gln Phe Ser Pro Asp
            580   585   590

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Trp Asn Gln Met Gln Lys Ile Phe Ala Asp Met Gln Gly Phe Thr Phe
    610   615   620

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Tyr Leu Val Leu Leu Glu Met Pro Phe Ser Pro Gln Leu Glu Ser Glu
                645   650   655

Tyr Glu Gln Val Lys Thr Thr Leu Lys Glu Gly Leu Gln Asn Ala Ser
            660   665   670

Gln Asp Ala Asn Ser Cys Gln Asp Ser Gln Thr Leu Cys Phe Lys Pro

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Asp Ser Ile Lys Val Asn Asn Asn Ser Lys Thr Glu Leu Thr Pro Glu
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Pro Leu Val Glu Ala Thr Arg Leu Arg Cys Val Thr Lys Cys Thr Ser
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Lys Gly Met Ile Gln Thr Arg Glu Asn Asp Lys Val Ile Val Lys Thr
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Leu Asp Asp Arg Met Leu Thr Leu Asn Asn Asp Gln Val Phe Pro Met
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Asn Pro Pro Lys Phe Asp Lys Ile Glu Asp Met Ala Met Met Thr His
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Leu His Glu Pro Ala Val Leu Tyr Asn Leu Lys Glu Arg Tyr Ala Ala
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Trp Met Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Thr Val Asn Pro
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Tyr Lys Trp Leu Pro Val Tyr Lys Pro Glu Val Val Ala Ala Tyr Arg
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Gly Lys Lys Arg Gln Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp
145 150 155 160

Asn Ala Tyr Gln Phe Met Leu Thr Asp Arg Asp Asn Gln Ser Ile Leu
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Ile Thr Gly Glu Ser Gly Ala Gly Lys Thr Val Asn Thr Lys Arg Val
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Thr Gln Pro Gly Lys Met Gln Gly Thr Leu Glu Asp Gln Ile Ile Gln
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Ala Asn Pro Leu Leu Glu Ala Phe Gly Asn Ala Lys Thr Val Arg Asn
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Asp Asn Ser Ser Arg Phe Gly Lys Phe Ile Arg Ile His Phe Gly Ala
245 250 255

Thr Gly Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu Lys
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Ala Ile Asp Ile Leu Gly Phe Ser Ser Glu Glu Lys Val Gly Ile Tyr
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Lys Leu Thr Gly Ala Val Met His Tyr Gly Asn Met Lys Phe Lys Gln
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Lys Gln Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Val Ala Asp
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Lys Ala Gly Tyr Leu Met Gly Leu Asn Ser Ala Glu Met Leu Lys Gly
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Leu Cys Cys Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly
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Gln Asn Val Gln Gln Val Thr Asn Ser Val Gly Ala Leu Ala Lys Ala
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Val Tyr Glu Lys Met Phe Leu Trp Met Val Thr Arg Ile Asn Gln Gln
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Leu Asp Thr Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile
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Ala Gly Phe Glu Ile Phe Asp Phe Asn Ser Leu Glu Gln Leu Cys Ile
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Asn Phe Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe
485 490 495

Val Leu Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Glu Phe
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Ile Asp Phe Gly Met Asp Leu Ala Ala Cys Ile Glu Leu Ile Glu Lys
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Pro Met Gly Ile Phe Ser Ile Leu Glu Glu Glu Cys Met Phe Pro Lys
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Ala Thr Asp Thr Ser Phe Lys Asn Lys Leu Tyr Asp Gln His Leu Gly
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Lys Ser Asn Asn Phe Gln Lys Pro Lys Pro Ala Lys Gly Lys Ala Glu
565 570 575

Ala His Phe Ser Leu Val His Tyr Ala Gly Thr Val Asp Tyr Asn Ile
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Ala Gly Trp Leu Asp Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val
595 600 605

Gly Leu Tyr Gln Lys Ser Ser Leu Lys Leu Leu Ser Phe Leu Phe Ser
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Asn Tyr Ala Gly Ala Glu Thr Gly Asp Ser Gly Gly Ser Lys Lys Gly
625 630 635 640

Gly Lys Lys Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Val Phe Arg
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Glu Asn Leu Asn Lys Leu Met Thr Asn Leu Arg Ser Thr His Pro His
660 665 670

Phe Val Arg Cys Leu Ile Pro Asn Glu Thr Lys Thr Pro Gly Val Met
675 680 685

Asp His Tyr Leu Val Met His Gln Leu Arg Cys Asn Gly Val Leu Glu
690 695 700

Gly Ile Arg Ile Cys Arg Lys Gly Phe Pro Ser Arg Ile Leu Tyr Ala
705 710 715 720

Asp Phe Lys Gln Arg Tyr Arg Ile Leu Asn Ala Ser Ala Ile Pro Glu
725 730 735

Gly Gln Phe Ile Asp Ser Lys Asn Ala Ser Glu Lys Leu Leu Asn Ser
740 745 750

Ile Asp Val Asp Arg Glu Gln Phe Arg Phe Gly Asn Thr Lys Val Phe
755 760 765

Phe Lys Ala Gly Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Lys
770 775 780

Leu Val Thr Leu Met Thr Ser Thr Gln Ala Val Cys Arg Gly Tyr Leu
785 790 795 800

Met Arg Val Glu Phe Lys Lys Met Met Glu Arg Arg Asp Ser Ile Phe
805 810 815

Cys Ile Gln Tyr Asn Ile Arg Ser Phe Met Asn Val Lys His Trp Pro
820 825 830

Trp Met Asn Leu Phe Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu
835 840 845

Ala Glu Lys Glu Met Ala Thr Met Lys Glu Asp Phe Glu Arg Thr Lys
850 855 860

Glu Glu Leu Ala Arg Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys
865 870 875 880

Met Val Ser Leu Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln
885 890 895

Ser Glu Thr Glu Asn Leu Met Asp Ala Glu Glu Arg Cys Glu Gly Leu
900 905 910

Ile Lys Ser Lys Ile Leu Leu Glu Ala Lys Val Lys Glu Leu Thr Glu
915 920 925

Arg Leu Glu Glu Glu Glu Glu Met Asn Ser Glu Leu Val Ala Lys Lys
930 935 940

Arg Asn Leu Glu Asp Lys Cys Ser Ser Leu Lys Arg Asp Ile Asp Asp

945 950 955 960

Leu Glu Leu Thr Leu Thr Lys Val Glu Lys Glu Lys His Ala Thr Glu
965 970 975

Asn Lys Val Lys Asn Leu Ser Glu Glu Met Thr Ala Leu Glu Glu Asn
980 985 990

Ile Ser Lys Leu Thr Lys Glu Lys Lys Ser Leu Gln Glu Ala His Gln
995 1000 1005

Gln Thr Leu Asp Asp Leu Gln Val Glu Glu Asp Lys Val Asn Gly
1010 1015 1020

Leu Ile Lys Ile Asn Ala Lys Leu Glu Gln Gln Thr Asp Asp Leu
1025 1030 1035

Glu Gly Ser Leu Glu Gln Glu Lys Lys Leu Arg Ala Asp Leu Glu
1040 1045 1050

Arg Ala Lys Arg Lys Leu Glu Gly Asp Leu Lys Met Ser Gln Glu
1055 1060 1065

Ser Ile Met Asp Leu Glu Asn Glu Lys Gln Gln Ile Glu Glu Lys
1070 1075 1080

Leu Lys Lys Lys Glu Phe Glu Leu Ser Gln Leu Gln Ala Arg Ile
1085 1090 1095

Asp Asp Glu Gln Val His Ser Leu Gln Phe Gln Lys Lys Ile Lys
1100 1105 1110

Glu Leu Gln Ala Arg Ile Glu Glu Leu Glu Glu Glu Ile Glu Ala
1115 1120 1125

Glu His Thr Leu Arg Ala Lys Ile Glu Lys Gln Arg Ser Asp Leu
1130 1135 1140

Ala Arg Glu Leu Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Ser
1145 1150 1155

Gly Ala Thr Ser Ala Gln Ile Glu Met Asn Lys Lys Arg Glu Ala
1160 1165 1170

Glu Phe Gln Lys Met Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln
1175 1180 1185

His Glu Ala Thr Ala Ala Thr Leu Arg Lys Lys Gln Ala Asp Ser
1190 1195 1200

Val Ala Glu Leu Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys
1205 1210 1215

Gln Lys Leu Glu Lys Glu Lys Ser Glu Leu Lys Met Glu Ile Asp
1220 1225 1230

Asp Met Ala Ser Asn Ile Glu Ala Leu Ser Lys Ser Lys Ser Asn
1235 1240 1245

Ile Glu Arg Thr Cys Arg Thr Val Glu Asp Gln Phe Ser Glu Ile
1250 1255 1260

Lys Ala Lys Asp Glu Gln Gln Thr Gln Leu Ile His Asp Leu Asn
1265 1270 1275

Met Gln Lys Ala Arg Leu Gln Thr Gln Asn Gly Glu Leu Ser His
1280 1285 1290

Arg Val Glu Glu Lys Glu Ser Leu Ile Ser Gln Leu Thr Lys Ser
1295 1300 1305

Lys Gln Ala Leu Thr Gln Gln Leu Glu Glu Leu Lys Arg Gln Met
1310 1315 1320

Glu Glu Glu Thr Lys Ala Lys Asn Ala Met Ala His Ala Leu Gln
1325 1330 1335

Ser Ser Arg His Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu
1340 1345 1350

Glu Gln Glu Ala Lys Ala Glu Leu Gln Arg Ala Leu Ser Lys Ala
1355 1360 1365

Asn Ser Glu Val Ala Gln Trp Lys Thr Lys Tyr Glu Thr Asp Ala
1370 1375 1380

Ile Gln Arg Thr Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala
1385 1390 1395

Gln Arg Leu Gln Glu Ala Glu Glu Lys Thr Glu Thr Ala Asn Ser
1400 1405 1410

Lys Cys Ala Ser Leu Glu Lys Thr Lys Gln Arg Leu Gln Gly Glu
1415 1420 1425

Val Glu Asp Leu Met Arg Asp Leu Glu Arg Ser His Thr Ala Cys
1430 1435 1440

Ala Thr Leu Asp Lys Lys Gln Arg Asn Phe Asp Lys Val Leu Ala
1445 1450 1455

Glu Trp Lys Gln Lys Leu Asp Glu Ser Gln Ala Glu Leu Glu Ala
1460 1465 1470

Ala Gln Lys Glu Ser Arg Ser Leu Ser Thr Glu Leu Phe Lys Met
1475 1480 1485

Arg Asn Ala Tyr Glu Glu Val Val Asp Gln Leu Glu Thr Leu Arg
1490 1495 1500

Arg Glu Asn Lys Asn Leu Gln Glu Glu Ile Ser Asp Leu Thr Glu
1505 1510 1515

Gln Ile Ala Glu Thr Gly Lys Asn Leu Gln Glu Ala Glu Lys Thr
1520 1525 1530

Lys Lys Leu Val Glu Gln Glu Lys Ser Asp Leu Gln Val Ala Leu
1535 1540 1545

Glu Glu Val Glu Gly Ser Leu Glu His Glu Glu Ser Lys Ile Leu
1550 1555 1560

Arg Val Gln Leu Glu Leu Ser Gln Val Lys Ser Glu Leu Asp Arg
1565 1570 1575

Lys Val Ile Glu Lys Asp Glu Glu Ile Glu Gln Leu Lys Arg Asn
1580 1585 1590

Ser Gln Arg Ala Ala Glu Ala Leu Gln Ser Val Leu Asp Ala Glu
1595 1600 1605

Ile Arg Ser Arg Asn Asp Ala Leu Arg Leu Lys Lys Lys Met Glu
1610 1615 1620

Gly Asp Leu Asn Glu Met Glu Ile Gln Leu Gly His Ser Asn Arg
1625 1630 1635

Gln Met Ala Glu Thr Gln Arg His Leu Arg Thr Val Gln Gly Gln
1640 1645 1650

Leu Lys Asp Ser Gln Leu His Leu Asp Asp Ala Leu Arg Ser Asn
1655 1660 1665

Glu Asp Leu Lys Glu Gln Leu Ala Ile Val Glu Arg Arg Asn Gly
1670 1675 1680

Leu Leu Leu Glu Glu Leu Glu Glu Met Lys Val Ala Leu Glu Gln
1685 1690 1695

Thr Glu Arg Thr Arg Arg Leu Ser Glu Gln Glu Leu Leu Asp Ala
1700 1705 1710

Ser Asp Arg Val Gln Leu Leu His Ser Gln Asn Thr Ser Leu Ile
1715 1720 1725

Asn Thr Lys Lys Lys Leu Glu Ala Asp Ile Ala Gln Cys Gln Ala
1730 1735 1740

Glu Val Glu Asn Ser Ile Gln Glu Ser Arg Asn Ala Glu Glu Lys
1745 1750 1755

Ala Lys Lys Ala Ile Thr Asp Ala Ala Met Met Ala Glu Glu Leu
1760 1765 1770

Lys Lys Glu Gln Asp Thr Ser Ala His Leu Glu Arg Met Lys Lys
1775 1780 1785

Asn Leu Glu Gln Thr Val Lys Asp Leu Gln His Arg Leu Asp Glu
1790 1795 1800

Ala Glu Gln Leu Ala Leu Lys Gly Gly Lys Lys Gln Ile Gln Lys
1805 1810 1815

Leu Glu Asn Arg Val Arg Glu Leu Glu Asn Glu Leu Asp Val Glu
1820 1825 1830

Gln Lys Arg Gly Ala Glu Ala Leu Lys Gly Ala His Lys Tyr Glu

1835 1840 1845

Arg Lys Val Lys Glu Met Thr Tyr Gln Ala Glu Glu Asp Arg Lys
1850 1855 1860

Asn Ile Leu Arg Leu Gln Asp Leu Val Asp Lys Leu Gln Ala Lys
1865 1870 1875

Val Lys Ser Tyr Lys Arg Gln Ala Glu Glu Ala Glu Glu Gln Ala
1880 1885 1890

Asn Thr Gln Leu Ser Arg Cys Arg Arg Val Gln His Glu Leu Glu
1895 1900 1905

Glu Ala Ala Glu Arg Ala Asp Ile Ala Glu Ser Gln Val Asn Lys
1910 1915 1920

Leu Arg Ala Lys Ser Arg Asp Val Gly Ser Gln Lys Met Glu Glu
1925 1930 1935

<210> 154
<211> 173
<212> PRT
<213> Human

<400> 154

Met Ala Ser Arg Lys Thr Lys Lys Lys Glu Gly Gly Ala Leu Arg Ala
1 5 10 15

Gln Arg Ala Ser Ser Asn Val Phe Ser Asn Phe Glu Gln Thr Gln Ile
20 25 30

Gln Glu Phe Lys Glu Ala Phe Thr Leu Met Asp Gln Asn Arg Asp Gly
35 40 45

Phe Ile Asp Lys Glu Asp Leu Lys Asp Thr Tyr Ala Ser Leu Gly Lys
50 55 60

Thr Asn Val Lys Asp Asp Glu Leu Asp Ala Met Leu Lys Glu Ala Ser
65 70 75 80

Gly Pro Ile Asn Phe Thr Met Phe Leu Asn Leu Phe Gly Glu Lys Leu
85 90 95

Ser Gly Thr Asp Ala Glu Glu Thr Ile Leu Asn Ala Phe Lys Met Leu

100 105 110

Asp Pro Asp Gly Lys Gly Lys Ile Asn Lys Glu Tyr Ile Lys Arg Leu
115 120 125

Leu Met Ser Gln Ala Asp Lys Met Thr Ala Glu Glu Val Asp Gln Met
130 135 140

Phe Gln Phe Ala Ser Ile Asp Val Ala Gly Asn Leu Asp Tyr Lys Ala
145 150 155 160

Leu Ser Tyr Val Ile Thr His Gly Glu Glu Lys Glu Glu
165 170

<210> 155
<211> 984
<212> PRT
<213> Human

<400> 155

Met Glu Thr Lys Gly Tyr His Ser Leu Pro Glu Gly Leu Asp Met Glu
1 5 10 15

Arg Arg Trp Gly Gln Val Ser Gln Ala Val Glu Arg Ser Ser Leu Gly
20 25 30

Pro Thr Glu Arg Thr Asp Glu Asn Asn Tyr Met Glu Ile Val Asn Val
35 40 45

Ser Cys Val Ser Gly Ala Ile Pro Asn Asn Ser Thr Gln Gly Ser Ser
50 55 60

Lys Glu Lys Gln Glu Leu Leu Pro Cys Leu Gln Gln Asp Asn Asn Arg
65 70 75 80

Pro Gly Ile Leu Thr Ser Asp Ile Lys Thr Glu Leu Glu Ser Lys Glu
85 90 95

Leu Ser Ala Thr Val Ala Glu Ser Met Gly Leu Tyr Met Asp Ser Val
100 105 110

Arg Asp Ala Asp Tyr Ser Tyr Glu Gln Gln Asn Gln Gln Gly Ser Met
115 120 125

Ser Pro Ala Lys Ile Tyr Gln Asn Val Glu Gln Leu Val Lys Phe Tyr

130 135 140

Lys Gly Asn Gly His Arg Pro Ser Thr Leu Ser Cys Val Asn Thr Pro
145 150 155 160

Leu Arg Ser Phe Met Ser Asp Ser Gly Ser Ser Val Asn Gly Gly Val
165 170 175

Met Arg Ala Ile Val Lys Ser Pro Ile Met Cys His Glu Lys Ser Pro
180 185 190

Ser Val Cys Ser Pro Leu Asn Met Thr Ser Ser Val Cys Ser Pro Ala
195 200 205

Gly Ile Asn Ser Val Ser Ser Thr Thr Ala Ser Phe Gly Ser Phe Pro
210 215 220

Val His Ser Pro Ile Thr Gln Gly Thr Pro Leu Thr Cys Ser Pro Asn
225 230 235 240

Ala Glu Asn Arg Gly Ser Arg Ser His Ser Pro Ala His Ala Ser Asn
245 250 255

Val Gly Ser Pro Leu Ser Ser Pro Leu Ser Ser Met Lys Ser Ser Ile
260 265 270

Ser Ser Pro Pro Ser His Cys Ser Val Lys Ser Pro Val Ser Ser Pro
275 280 285

Asn Asn Val Thr Leu Arg Ser Ser Val Ser Ser Pro Ala Asn Ile Asn
290 295 300

Asn Ser Arg Cys Ser Val Ser Ser Pro Ser Asn Thr Asn Asn Arg Ser
305 310 315 320

Thr Leu Ser Ser Pro Ala Ala Ser Thr Val Gly Ser Ile Cys Ser Pro
325 330 335

Val Asn Asn Ala Phe Ser Tyr Thr Ala Ser Gly Thr Ser Ala Gly Ser
340 345 350

Ser Thr Leu Arg Asp Val Val Pro Ser Pro Asp Thr Gln Glu Lys Gly
355 360 365

Ala Gln Glu Val Pro Phe Pro Lys Thr Glu Glu Val Glu Ser Ala Ile
370 375 380

Ser Asn Gly Val Thr Gly Gln Leu Asn Ile Val Gln Tyr Ile Lys Pro
385 390 395 400

Glu Pro Asp Gly Ala Phe Ser Ser Ser Cys Leu Gly Gly Asn Ser Lys
405 410 415

Ile Asn Ser Asp Ser Ser Phe Ser Val Pro Ile Lys Gln Glu Ser Thr
420 425 430

Lys His Ser Cys Ser Gly Thr Ser Phe Lys Gly Asn Pro Thr Val Asn
435 440 445

Pro Phe Pro Phe Met Asp Gly Ser Tyr Phe Ser Phe Met Asp Asp Lys
450 455 460

Asp Tyr Tyr Ser Leu Ser Gly Ile Leu Gly Pro Pro Val Pro Gly Phe
465 470 475 480

Asp Gly Asn Cys Glu Gly Ser Gly Phe Pro Val Gly Ile Lys Gln Glu
485 490 495

Pro Asp Asp Gly Ser Tyr Tyr Pro Glu Ala Ser Ile Pro Ser Ser Ala
500 505 510

Ile Val Gly Val Asn Ser Gly Gly Gln Ser Phe His Tyr Arg Ile Gly
515 520 525

Ala Gln Gly Thr Ile Ser Leu Ser Arg Ser Ala Arg Asp Gln Ser Phe
530 535 540

Gln His Leu Ser Ser Phe Pro Pro Val Asn Thr Leu Val Glu Ser Trp
545 550 555 560

Lys Ser His Gly Asp Leu Ser Ser Arg Arg Ser Asp Gly Tyr Pro Val
565 570 575

Leu Glu Tyr Ile Pro Glu Asn Val Ser Ser Ser Thr Leu Arg Ser Val
580 585 590

Ser Thr Gly Ser Ser Arg Pro Ser Lys Ile Cys Leu Val Cys Gly Asp
595 600 605

Glu Ala Ser Gly Cys His Tyr Gly Val Val Thr Cys Gly Ser Cys Lys
610 615 620

Val Phe Phe Lys Arg Ala Val Glu Gly Gln His Asn Tyr Leu Cys Ala
625 630 635 640

Gly Arg Asn Asp Cys Ile Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro
645 650 655

Ala Cys Arg Leu Gln Lys Cys Leu Gln Ala Gly Met Asn Leu Gly Ala
660 665 670

Arg Lys Ser Lys Lys Leu Gly Lys Leu Lys Gly Ile His Glu Glu Gln
675 680 685

Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro Gln Ser Pro
690 695 700

Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro Ser Val Asn
705 710 715 720

Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala Leu Thr Pro
725 730 735

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
740 745 750

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
755 760 765

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
770 775 780

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
785 790 795 800

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
805 810 815

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
820 825 830

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
835 840 845

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
    850   855   860

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
865   870   875   880

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
                885   890   895

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
            900   905   910

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
        915   920   925

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
    930   935   940

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
945   950   955   960

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
                965   970   975

Lys Pro Leu Tyr Phe His Arg Lys
            980

<210> 156
<211> 495
<212> PRT
<213> Human

<400> 156

Met Ser Ser Asn Ser Asp Thr Gly Asp Leu Gln Glu Ser Leu Lys His
1   5   10   15

Gly Leu Thr Pro Ile Val Ser Gln Phe Lys Met Val Asn Tyr Ser Tyr
            20   25   30

Asp Glu Asp Leu Glu Glu Leu Cys Pro Val Cys Gly Asp Lys Val Ser
        35   40   45

Gly Tyr His Tyr Gly Leu Leu Thr Cys Glu Ser Cys Lys Gly Phe Phe
    50   55   60

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Lys Arg Thr Val Gln Asn Asn Lys Arg Tyr Thr Cys Ile Glu Asn Gln
65                  70                  75                  80

Asn Cys Gln Ile Asp Lys Thr Gln Arg Lys Arg Cys Pro Tyr Cys Arg
                85                  90                  95

Phe Gln Lys Cys Leu Ser Val Gly Met Lys Leu Glu Ala Val Arg Ala
            100                 105                 110

Asp Arg Met Arg Gly Gly Arg Asn Lys Phe Gly Pro Met Tyr Lys Arg
        115                 120                 125

Asp Arg Ala Leu Lys Gln Gln Lys Lys Ala Leu Ile Arg Ala Asn Gly
    130                 135                 140

Leu Lys Leu Glu Ala Met Ser Gln Val Ile Gln Ala Met Pro Ser Asp
145                 150                 155                 160

Leu Thr Ile Ser Ser Ala Ile Gln Asn Ile His Ser Ala Ser Lys Gly
                165                 170                 175

Leu Pro Leu Asn His Ala Ala Leu Pro Pro Thr Asp Tyr Asp Arg Ser
            180                 185                 190

Pro Phe Val Thr Ser Pro Ile Ser Met Thr Met Pro Pro His Gly Ser
        195                 200                 205

Leu Gln Gly Tyr Gln Thr Tyr Gly His Phe Pro Ser Arg Ala Ile Lys
    210                 215                 220

Ser Glu Tyr Pro Asp Pro Tyr Thr Ser Ser Pro Glu Ser Ile Met Gly
225                 230                 235                 240

Tyr Ser Tyr Met Asp Ser Tyr Gln Thr Ser Ser Pro Ala Ser Ile Pro
                245                 250                 255

His Leu Ile Leu Glu Leu Leu Lys Cys Glu Pro Asp Glu Pro Gln Val
            260                 265                 270

Gln Ala Lys Ile Met Ala Tyr Leu Gln Gln Glu Gln Ala Asn Arg Ser
        275                 280                 285

Lys His Glu Lys Leu Ser Thr Phe Gly Leu Met Cys Lys Met Ala Asp
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290 295 300

Gln Thr Leu Phe Ser Ile Val Glu Trp Ala Arg Ser Ser Ile Phe Phe
305 310 315 320

Arg Glu Leu Lys Val Asp Asp Gln Met Lys Leu Leu Gln Asn Cys Trp
325 330 335

Ser Glu Leu Leu Ile Leu Asp His Ile Tyr Arg Gln Val Val His Gly
340 345 350

Lys Glu Gly Ser Ile Phe Leu Val Thr Gly Gln Gln Val Asp Tyr Ser
355 360 365

Ile Ile Ala Ser Gln Ala Gly Ala Thr Leu Asn Asn Leu Met Ser His
370 375 380

Ala Gln Glu Leu Val Ala Lys Leu Arg Ser Leu Gln Phe Asp Gln Arg
385 390 395 400

Glu Phe Val Cys Leu Lys Phe Leu Val Leu Phe Ser Leu Asp Val Lys
405 410 415

Asn Leu Glu Asn Phe Gln Leu Val Glu Gly Val Gln Glu Gln Val Asn
420 425 430

Ala Ala Leu Leu Asp Tyr Thr Met Cys Asn Tyr Pro Gln Gln Thr Glu
435 440 445

Lys Phe Gly Gln Leu Leu Leu Arg Leu Pro Glu Ile Arg Ala Ile Ser
450 455 460

Met Gln Ala Glu Glu Tyr Leu Tyr Tyr Lys His Leu Asn Gly Asp Val
465 470 475 480

Pro Tyr Asn Asn Leu Leu Ile Glu Met Leu His Ala Lys Arg Ala
485 490 495

<210> 157
<211> 2303
<212> PRT
<213> Human

<400> 157

Met Thr Ser Glu Glu Met Thr Ala Ser Val Leu Ile Pro Val Thr Gln

1 5 10 15

Arg Lys Val Val Ser Ala Gln Ser Ala Ala Asp Glu Ser Ser Glu Lys
20 25 30

Val Ser Asp Ile Asn Ile Ser Lys Ala His Thr Val Arg Arg Ser Gly
35 40 45

Glu Thr Ser His Thr Ile Ser Gln Leu Asn Lys Leu Lys Glu Glu Pro
50 55 60

Ser Gly Ser Asn Leu Pro Lys Ile Leu Ser Ile Ala Arg Glu Lys Ile
65 70 75 80

Val Ser Asp Glu Asn Ser Asn Glu Lys Cys Trp Glu Lys Ile Met Pro
85 90 95

Asp Ser Ala Lys Asn Leu Asn Ile Asn Cys Asn Asn Ile Leu Arg Asn
100 105 110

His Gln His Gly Leu Pro Gln Arg Gln Phe Tyr Glu Met Tyr Asn Ser
115 120 125

Val Ala Glu Glu Asp Leu Cys Leu Glu Thr Gly Ile Pro Ser Pro Leu
130 135 140

Glu Arg Lys Val Phe Pro Gly Ile Gln Leu Glu Leu Asp Arg Pro Ser
145 150 155 160

Met Gly Ile Ser Pro Leu Gly Asn Gln Ser Val Ile Ile Glu Thr Gly
165 170 175

Arg Ala His Pro Asp Ser Arg Arg Ala Val Phe His Phe His Tyr Glu
180 185 190

Val Asp Arg Arg Met Ser Asp Thr Phe Cys Thr Leu Ser Glu Asn Leu
195 200 205

Ile Leu Asp Asp Cys Gly Asn Cys Val Pro Leu Pro Gly Gly Glu Glu
210 215 220

Lys Gln Lys Lys Asn Tyr Val Ala Tyr Thr Cys Lys Leu Met Glu Leu
225 230 235 240

Ala Lys Asn Cys Asp Asn Lys Asn Glu Gln Leu Gln Cys Asp His Cys
245 250 255

Asp Thr Leu Asn Asp Lys Tyr Phe Cys Phe Glu Gly Ser Cys Glu Lys
260 265 270

Val Asp Met Val Tyr Ser Gly Asp Ser Phe Cys Arg Lys Asp Phe Thr
275 280 285

Asp Ser Gln Ala Ala Lys Thr Phe Leu Ser His Phe Glu Asp Phe Pro
290 295 300

Asp Asn Cys Asp Asp Val Glu Glu Asp Ala Phe Lys Ser Lys Lys Glu
305 310 315 320

Arg Ser Thr Leu Leu Val Arg Arg Phe Cys Lys Asn Asp Arg Glu Val
325 330 335

Lys Lys Ser Val Tyr Thr Gly Thr Arg Ala Ile Val Arg Thr Leu Pro
340 345 350

Ser Gly His Ile Gly Leu Thr Ala Trp Ser Tyr Ile Asp Gln Lys Arg
355 360 365

Asn Gly Pro Leu Leu Pro Cys Gly Arg Val Met Glu Pro Pro Ser Thr
370 375 380

Val Glu Ile Arg Gln Asp Gly Ser Gln Arg Leu Ser Glu Ala Gln Trp
385 390 395 400

Tyr Pro Ile Tyr Asn Ala Val Arg Arg Glu Glu Thr Glu Asn Thr Val
405 410 415

Gly Ser Leu Leu His Phe Leu Thr Lys Leu Pro Ala Ser Glu Thr Ala
420 425 430

His Gly Arg Ile Ser Val Gly Pro Cys Leu Lys Gln Cys Val Arg Asp
435 440 445

Thr Val Cys Glu Tyr Arg Ala Thr Leu Gln Arg Thr Ser Ile Ser Gln
450 455 460

Tyr Ile Thr Gly Ser Leu Leu Glu Ala Thr Thr Ser Leu Gly Ala Arg
465 470 475 480

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Ser Gly Leu Leu Ser Thr Phe Gly Gly Ser Thr Gly Arg Met Met Leu
                485                 490                 495

Lys Glu Arg Gln Pro Gly Pro Ser Val Ala Asn Ser Asn Ala Leu Pro
            500                 505                 510

Ser Ser Ser Ala Gly Ile Ser Lys Glu Leu Ile Asp Leu Gln Pro Leu
        515                 520                 525

Ile Gln Phe Pro Glu Glu Val Ala Ser Ile Leu Met Glu Gln Glu Gln
    530                 535                 540

Thr Ile Tyr Arg Arg Val Leu Pro Val Asp Tyr Leu Cys Phe Leu Thr
545                 550                 555                 560

Arg Asp Leu Gly Thr Pro Glu Cys Gln Ser Ser Leu Pro Cys Leu Lys
                565                 570                 575

Ala Ser Ile Ser Ala Ser Ile Leu Thr Thr Gln Asn Gly Glu His Asn
            580                 585                 590

Ala Leu Glu Asp Leu Val Met Arg Phe Asn Glu Val Ser Ser Trp Val
        595                 600                 605

Thr Trp Leu Ile Leu Thr Ala Gly Ser Met Glu Glu Lys Arg Glu Val
    610                 615                 620

Phe Ser Tyr Leu Val His Val Ala Lys Cys Cys Trp Asn Met Gly Asn
625                 630                 635                 640

Tyr Asn Ala Val Met Glu Phe Leu Ala Gly Leu Arg Ser Arg Lys Val
                645                 650                 655

Leu Lys Met Trp Gln Phe Met Asp Gln Ser Asp Ile Glu Thr Met Arg
            660                 665                 670

Ser Leu Lys Asp Ala Met Ala Gln His Glu Ser Ser Cys Glu Tyr Arg
        675                 680                 685

Lys Val Val Thr Arg Ala Leu His Ile Pro Gly Cys Lys Val Val Pro
    690                 695                 700

Phe Cys Gly Val Phe Leu Lys Glu Leu Cys Glu Val Leu Asp Gly Ala
705                 710                 715                 720
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Ser Gly Leu Met Lys Leu Cys Pro Arg Tyr Asn Ser Gln Glu Glu Thr
725 730 735

Leu Glu Phe Val Ala Asp Tyr Ser Gly Gln Asp Asn Phe Leu Gln Arg
740 745 750

Val Gly Gln Asn Gly Leu Lys Asn Ser Glu Lys Glu Ser Thr Val Asn
755 760 765

Ser Ile Phe Gln Val Ile Arg Ser Cys Asn Arg Ser Leu Glu Thr Asp
770 775 780

Glu Glu Asp Ser Pro Ser Glu Gly Asn Ser Ser Arg Lys Ser Ser Leu
785 790 795 800

Lys Asp Lys Ser Arg Trp Gln Phe Ile Ile Gly Asp Leu Leu Asp Ser
805 810 815

Asp Asn Asp Ile Phe Glu Gln Ser Lys Glu Tyr Asp Ser His Gly Ser
820 825 830

Glu Asp Ser Gln Lys Ala Phe Asp His Gly Thr Glu Leu Ile Pro Trp
835 840 845

Tyr Val Leu Ser Ile Gln Ala Asp Val His Gln Phe Leu Leu Gln Gly
850 855 860

Ala Thr Val Ile His Tyr Asp Gln Asp Thr His Leu Ser Ala Arg Cys
865 870 875 880

Phe Leu Gln Leu Gln Pro Asp Asn Ser Thr Leu Thr Trp Val Lys Pro
885 890 895

Thr Thr Ala Ser Pro Ala Ser Ser Lys Ala Lys Leu Gly Val Leu Asn
900 905 910

Asn Thr Ala Glu Pro Gly Lys Phe Pro Leu Leu Gly Asn Ala Gly Leu
915 920 925

Ser Ser Leu Thr Glu Gly Val Leu Asp Leu Phe Ala Val Lys Ala Val
930 935 940

Tyr Met Gly His Pro Gly Ile Asp Ile His Thr Val Cys Val Gln Asn

945 950 955 960

Lys Leu Gly Ser Met Phe Leu Ser Glu Thr Gly Val Thr Leu Leu Tyr
965 970 975

Gly Leu Gln Thr Thr Asp Asn Arg Leu Leu His Phe Val Ala Pro Lys
980 985 990

His Thr Ala Lys Met Leu Phe Ser Gly Leu Leu Glu Leu Thr Arg Ala
995 1000 1005

Val Arg Lys Met Arg Lys Phe Pro Asp Gln Arg Gln Gln Trp Leu
1010 1015 1020

Arg Lys Gln Tyr Val Ser Leu Tyr Gln Glu Asp Gly Arg Tyr Glu
1025 1030 1035

Gly Pro Thr Leu Ala His Ala Val Glu Leu Phe Gly Gly Arg Arg
1040 1045 1050

Trp Ser Ala Arg Asn Pro Ser Pro Gly Thr Ser Ala Lys Asn Ala
1055 1060 1065

Glu Lys Pro Asn Met Gln Arg Asn Asn Thr Leu Gly Ile Ser Thr
1070 1075 1080

Thr Lys Lys Lys Lys Lys Ile Leu Met Arg Gly Glu Ser Gly Glu
1085 1090 1095

Val Thr Asp Asp Glu Met Ala Thr Arg Lys Ala Lys Met His Lys
1100 1105 1110

Glu Cys Arg Ser Arg Ser Gly Ser Asp Pro Gln Asp Ile Asn Glu
1115 1120 1125

Gln Glu Glu Ser Glu Val Asn Ala Ile Ala Asn Pro Pro Asn Pro
1130 1135 1140

Leu Pro Ser Arg Arg Ala His Ser Leu Thr Thr Ala Gly Ser Pro
1145 1150 1155

Asn Leu Ala Ala Gly Thr Ser Ser Pro Ile Arg Pro Val Ser Ser
1160 1165 1170

Pro Val Leu Ser Ser Ser Asn Lys Ser Pro Ser Ser Ala Trp Ser
1175 1180 1185

Ser Ser Ser Trp His Gly Arg Ile Lys Gly Gly Met Lys Gly Phe
1190 1195 1200

Gln Ser Phe Met Val Ser Asp Ser Asn Met Ser Phe Val Glu Phe
1205 1210 1215

Val Glu Leu Phe Lys Ser Phe Ser Val Arg Ser Arg Lys Asp Leu
1220 1225 1230

Lys Asp Leu Phe Asp Val Tyr Ala Val Pro Cys Asn Arg Ser Gly
1235 1240 1245

Ser Glu Ser Ala Pro Leu Tyr Thr Asn Leu Thr Ile Asp Glu Asn
1250 1255 1260

Thr Ser Asp Leu Gln Pro Asp Leu Asp Leu Leu Thr Arg Asn Val
1265 1270 1275

Ser Asp Leu Gly Leu Phe Ile Lys Ser Lys Gln Gln Leu Ser Asp
1280 1285 1290

Asn Gln Arg Gln Ile Ser Asp Ala Ile Ala Ala Ala Ser Ile Val
1295 1300 1305

Thr Asn Gly Thr Gly Ile Glu Ser Thr Ser Leu Gly Ile Phe Gly
1310 1315 1320

Val Gly Ile Leu Gln Leu Asn Asp Phe Leu Val Asn Cys Gln Gly
1325 1330 1335

Glu His Cys Thr Tyr Asp Glu Ile Leu Ser Ile Ile Gln Lys Phe
1340 1345 1350

Glu Pro Ser Ile Ser Met Cys His Gln Gly Leu Met Ser Phe Glu
1355 1360 1365

Gly Phe Ala Arg Phe Leu Met Asp Lys Glu Asn Phe Ala Ser Lys
1370 1375 1380

Asn Asp Glu Ser Gln Glu Asn Ile Lys Glu Leu Gln Leu Pro Leu
1385 1390 1395

Ser Tyr Tyr Tyr Ile Glu Ser Ser His Asn Thr Tyr Leu Thr Gly
1400 1405 1410

His Gln Leu Lys Gly Glu Ser Ser Val Glu Leu Tyr Ser Gln Val
1415 1420 1425

Leu Leu Gln Gly Cys Arg Ser Val Glu Leu Asp Cys Trp Asp Gly
1430 1435 1440

Asp Asp Gly Met Pro Ile Ile Tyr His Gly His Thr Pro Thr Thr
1445 1450 1455

Lys Ile Pro Phe Lys Glu Val Val Glu Ala Ile Asp Arg Ser Ala
1460 1465 1470

Phe Ile Asn Ser Asp Leu Pro Ile Ile Ile Ser Ile Glu Asn His
1475 1480 1485

Cys Ser Leu Pro Gln Gln Arg Lys Met Ala Glu Ile Phe Lys Thr
1490 1495 1500

Val Phe Gly Glu Lys Leu Val Thr Lys Phe Leu Phe Glu Thr Asp
1505 1510 1515

Phe Ser Asp Asp Pro Met Leu Pro Ser Pro Asp Gln Leu Arg Lys
1520 1525 1530

Lys Val Leu Leu Lys Asn Lys Lys Leu Lys Ala His Gln Thr Pro
1535 1540 1545

Val Asp Ile Leu Lys Gln Lys Ala His Gln Leu Ala Ser Met Gln
1550 1555 1560

Val Gln Ala Tyr Asn Gly Gly Asn Ala Asn Pro Arg Pro Ala Asn
1565 1570 1575

Asn Glu Glu Glu Glu Asp Glu Glu Asp Glu Tyr Asp Tyr Asp Tyr
1580 1585 1590

Glu Ser Leu Ser Asp Asp Asn Ile Leu Glu Asp Arg Pro Glu Asn
1595 1600 1605

Lys Ser Cys Asn Asp Lys Leu Gln Phe Glu Tyr Asn Glu Glu Ile
1610 1615 1620

Pro Lys Arg Ile Lys Lys Ala Asp Asn Ser Ala Cys Asn Lys Gly
1625 1630 1635

Lys Val Tyr Asp Met Glu Leu Gly Glu Glu Phe Tyr Leu Asp Gln
1640 1645 1650

Asn Lys Lys Glu Ser Arg Gln Ile Ala Pro Glu Leu Ser Asp Leu
1655 1660 1665

Val Ile Tyr Arg Gln Ala Val Lys Phe Pro Gly Leu Ser Thr Leu
1670 1675 1680

Asn Ala Ser Gly Ser Ser Arg Gly Lys Glu Arg Lys Ser Arg Lys
1685 1690 1695

Ser Ile Phe Gly Asn Asn Pro Gly Arg Met Ser Pro Gly Glu Thr
1700 1705 1710

Ala Ser Phe Asn Lys Thr Ser Gly Lys Ser Ser Cys Glu Gly Ile
1715 1720 1725

Arg Gln Thr Trp Glu Glu Ser Ser Ser Pro Leu Asn Pro Thr Thr
1730 1735 1740

Ser Leu Ser Ala Ile Ile Arg Thr Pro Lys Cys Tyr His Ile Ser
1745 1750 1755

Ser Leu Asn Glu Asn Ala Ala Lys Arg Leu Cys Arg Arg Tyr Ser
1760 1765 1770

Gln Lys Leu Ile Gln His Thr Ala Cys Gln Leu Leu Arg Thr Tyr
1775 1780 1785

Pro Ala Ala Thr Arg Ile Asp Ser Ser Asn Pro Asn Pro Leu Met
1790 1795 1800

Phe Trp Leu His Gly Ile Gln Leu Val Ala Leu Asn Tyr Gln Thr
1805 1810 1815

Asp Asp Leu Pro Leu His Leu Asn Ala Ala Met Phe Glu Ala Asn
1820 1825 1830

Gly Gly Cys Gly Tyr Val Leu Lys Pro Pro Val Leu Trp Asp Lys

1835 1840 1845

Asn Cys Pro Met Tyr Gln Lys Phe Ser Pro Leu Glu Arg Asp Leu
1850 1855 1860

Asp Ser Met Asp Pro Ala Val Tyr Ser Leu Thr Ile Val Ser Gly
1865 1870 1875

Gln Asn Val Cys Pro Ser Asn Ser Met Gly Ser Pro Cys Ile Glu
1880 1885 1890

Val Asp Val Leu Gly Met Pro Leu Asp Ser Cys His Phe Arg Thr
1895 1900 1905

Lys Pro Ile His Arg Asn Thr Leu Asn Pro Met Trp Asn Glu Gln
1910 1915 1920

Phe Leu Phe Arg Val His Phe Glu Asp Leu Val Phe Leu Arg Phe
1925 1930 1935

Ala Val Val Glu Asn Asn Ser Ser Ala Val Thr Ala Gln Arg Ile
1940 1945 1950

Ile Pro Leu Lys Ala Leu Lys Arg Gly Tyr Arg His Leu Gln Leu
1955 1960 1965

Arg Asn Leu His Asn Glu Val Leu Glu Ile Ser Ser Leu Phe Ile
1970 1975 1980

Asn Ser Arg Arg Met Glu Glu Asn Ser Ser Gly Asn Thr Met Ser
1985 1990 1995

Ala Ser Ser Met Phe Asn Thr Glu Glu Arg Lys Cys Leu Gln Thr
2000 2005 2010

His Arg Val Thr Val His Gly Val Pro Gly Pro Glu Pro Phe Thr
2015 2020 2025

Val Phe Thr Ile Asn Gly Gly Thr Lys Ala Lys Gln Leu Leu Gln
2030 2035 2040

Gln Ile Leu Thr Asn Glu Gln Asp Ile Lys Pro Val Thr Thr Asp
2045 2050 2055

Tyr Phe Leu Met Glu Glu Lys Tyr Phe Ile Ser Lys Glu Lys Asn
2060 2065 2070

Glu Cys Arg Lys Gln Pro Phe Gln Arg Ala Ile Gly Pro Glu Glu
2075 2080 2085

Glu Ile Met Gln Ile Leu Ser Ser Trp Phe Pro Glu Glu Gly Tyr
2090 2095 2100

Met Gly Arg Ile Val Leu Lys Thr Gln Gln Glu Asn Leu Glu Glu
2105 2110 2115

Lys Asn Ile Val Gln Asp Asp Lys Glu Val Ile Leu Ser Ser Glu
2120 2125 2130

Glu Glu Ser Phe Phe Val Gln Val His Asp Val Ser Pro Glu Gln
2135 2140 2145

Pro Arg Thr Val Ile Lys Ala Pro Arg Val Ser Thr Ala Gln Asp
2150 2155 2160

Val Ile Gln Gln Thr Leu Cys Lys Ala Lys Tyr Ser Tyr Ser Ile
2165 2170 2175

Leu Ser Asn Pro Asn Pro Ser Asp Tyr Val Leu Leu Glu Glu Val
2180 2185 2190

Val Lys Asp Thr Thr Asn Lys Lys Thr Thr Thr Pro Lys Ser Ser
2195 2200 2205

Gln Arg Val Leu Leu Asp Gln Glu Cys Val Phe Gln Ala Gln Ser
2210 2215 2220

Lys Trp Lys Gly Ala Gly Lys Phe Ile Leu Lys Leu Lys Glu Gln
2225 2230 2235

Val Gln Ala Ser Arg Glu Asp Lys Lys Lys Gly Ile Ser Phe Ala
2240 2245 2250

Ser Glu Leu Lys Lys Leu Thr Lys Ser Thr Lys Gln Pro Arg Gly
2255 2260 2265

Leu Thr Ser Pro Ser Gln Leu Leu Thr Ser Glu Ser Ile Gln Thr
2270 2275 2280

Lys Glu Glu Lys Pro Val Gly Gly Leu Ser Pro Val Thr Gln Trp
2285 2290 2295

Ile Thr Asp Ser Asp
2300

<210> 158
<211> 303
<212> PRT
<213> Human

<400> 158

Met Ala Ser Trp Ala Lys Gly Arg Ser Tyr Leu Ala Pro Gly Leu Leu
1 5 10 15

Gln Gly Gln Val Ala Ile Val Thr Gly Gly Ala Thr Gly Ile Gly Lys
20 25 30

Ala Ile Val Lys Glu Leu Leu Glu Leu Gly Ser Asn Val Val Ile Ala
35 40 45

Ser Arg Lys Leu Glu Arg Leu Lys Ser Ala Ala Asp Glu Leu Gln Ala
50 55 60

Asn Leu Pro Pro Thr Lys Gln Ala Arg Val Ile Pro Ile Gln Cys Asn
65 70 75 80

Ile Arg Asn Glu Glu Glu Val Asn Asn Leu Val Lys Ser Thr Leu Asp
85 90 95

Thr Phe Gly Lys Ile Asn Phe Leu Val Asn Asn Gly Gly Gly Gln Phe
100 105 110

Leu Ser Pro Ala Glu His Ile Ser Ser Lys Gly Trp His Ala Val Leu
115 120 125

Glu Thr Asn Leu Thr Gly Thr Phe Tyr Met Cys Lys Ala Val Tyr Ser
130 135 140

Ser Trp Met Lys Glu His Gly Gly Ser Ile Val Asn Ile Ile Val Pro
145 150 155 160

Thr Lys Ala Gly Phe Pro Leu Ala Val His Ser Gly Ala Ala Arg Ala
165 170 175

Gly Val Tyr Asn Leu Thr Lys Ser Leu Ala Leu Glu Trp Ala Cys Ser
180 185 190

Gly Ile Arg Ile Asn Cys Val Ala Pro Gly Val Ile Tyr Ser Gln Thr
195 200 205

Ala Val Glu Asn Tyr Gly Ser Trp Gly Gln Ser Phe Phe Glu Gly Ser
210 215 220

Phe Gln Lys Ile Pro Ala Lys Arg Ile Gly Val Pro Glu Glu Val Ser
225 230 235 240

Ser Val Val Cys Phe Leu Leu Ser Pro Ala Ala Ser Phe Ile Thr Gly
245 250 255

Gln Ser Val Asp Val Asp Gly Gly Arg Ser Leu Tyr Thr His Ser Tyr
260 265 270

Glu Val Pro Asp His Asp Asn Trp Pro Lys Gly Ala Gly Asp Leu Ser
275 280 285

Val Val Lys Lys Met Lys Glu Thr Phe Lys Glu Lys Ala Lys Leu
290 295 300

<210> 159
<211> 246
<212> PRT
<213> Human

<400> 159

Met Glu Glu Ala Lys Ser Gln Ser Leu Glu Glu Asp Phe Glu Gly Gln
1 5 10 15

Ala Thr His Thr Gly Pro Lys Gly Val Ile Asn Asp Trp Arg Lys Phe
20 25 30

Lys Leu Glu Ser Gln Asp Ser Asp Ser Ile Pro Pro Ser Lys Lys Glu
35 40 45

Ile Leu Arg Gln Met Ser Ser Pro Gln Ser Arg Asn Gly Lys Asp Ser
50 55 60

Lys Glu Arg Val Ser Arg Lys Met Ser Ile Gln Glu Tyr Glu Leu Ile
65 70 75 80

His Lys Glu Lys Glu Asp Glu Asn Cys Leu Arg Lys Tyr Arg Arg Gln
85 90 95

Cys Met Gln Asp Met His Gln Lys Leu Ser Phe Gly Pro Arg Tyr Gly
100 105 110

Phe Val Tyr Glu Leu Glu Thr Gly Lys Gln Phe Leu Glu Thr Ile Glu
115 120 125

Lys Glu Leu Lys Ile Thr Thr Ile Val Val His Ile Tyr Glu Asp Gly
130 135 140

Ile Lys Gly Cys Asp Ala Leu Asn Ser Ser Leu Thr Cys Leu Ala Ala
145 150 155 160

Glu Tyr Pro Ile Val Lys Phe Cys Lys Ile Lys Ala Ser Asn Thr Gly
165 170 175

Ala Gly Asp Arg Phe Ser Leu Asp Val Leu Pro Thr Leu Leu Ile Tyr
180 185 190

Lys Gly Gly Glu Leu Ile Ser Asn Phe Ile Ser Val Ala Glu Gln Phe
195 200 205

Ala Glu Glu Phe Phe Ala Gly Asp Val Glu Ser Phe Leu Asn Glu Tyr
210 215 220

Gly Leu Leu Pro Glu Arg Glu Val His Val Leu Glu His Thr Lys Ile
225 230 235 240

Glu Glu Glu Asp Val Glu
245

<210> 160
<211> 403
<212> PRT
<213> Human

<400> 160

Met Thr Ala Ile Ile Lys Glu Ile Val Ser Arg Asn Lys Arg Arg Tyr
1 5 10 15

Gln Glu Asp Gly Phe Asp Leu Asp Leu Thr Tyr Ile Tyr Pro Asn Ile
20 25 30

Ile Ala Met Gly Phe Pro Ala Glu Arg Leu Glu Gly Val Tyr Arg Asn
35 40 45

Asn Ile Asp Asp Val Val Arg Phe Leu Asp Ser Lys His Lys Asn His
50 55 60

Tyr Lys Ile Tyr Asn Leu Cys Ala Glu Arg His Tyr Asp Thr Ala Lys
65 70 75 80

Phe Asn Cys Arg Val Ala Gln Tyr Pro Phe Glu Asp His Asn Pro Pro
85 90 95

Gln Leu Glu Leu Ile Lys Pro Phe Cys Glu Asp Leu Asp Gln Trp Leu
100 105 110

Ser Glu Asp Asp Asn His Val Ala Ala Ile His Cys Lys Ala Gly Lys
115 120 125

Gly Arg Thr Gly Val Met Ile Cys Ala Tyr Leu Leu His Arg Gly Lys
130 135 140

Phe Leu Lys Ala Gln Glu Ala Leu Asp Phe Tyr Gly Glu Val Arg Thr
145 150 155 160

Arg Asp Lys Lys Gly Val Thr Ile Pro Ser Gln Arg Arg Tyr Val Tyr
165 170 175

Tyr Tyr Ser Tyr Leu Leu Lys Asn His Leu Asp Tyr Arg Pro Val Ala
180 185 190

Leu Leu Phe His Lys Met Met Phe Glu Thr Ile Pro Met Phe Ser Gly
195 200 205

Gly Thr Cys Asn Pro Gln Phe Val Val Cys Gln Leu Lys Val Lys Ile
210 215 220

Tyr Ser Ser Asn Ser Gly Pro Thr Arg Arg Glu Asp Lys Phe Met Tyr
225 230 235 240

Phe Glu Phe Pro Gln Pro Leu Pro Val Cys Gly Asp Ile Lys Val Glu
245 250 255

Phe Phe His Lys Gln Asn Lys Met Leu Lys Lys Asp Lys Met Phe His
260 265 270

Phe Trp Val Asn Thr Phe Phe Ile Pro Gly Pro Glu Glu Thr Ser Glu
275 280 285

Lys Val Glu Asn Gly Ser Leu Cys Asp Gln Glu Ile Asp Ser Ile Cys
290 295 300

Ser Ile Glu Arg Ala Asp Asn Asp Lys Glu Tyr Leu Val Leu Thr Leu
305 310 315 320

Thr Lys Asn Asp Leu Asp Lys Ala Asn Lys Asp Lys Ala Asn Arg Tyr
325 330 335

Phe Ser Pro Asn Phe Lys Val Lys Leu Tyr Phe Thr Lys Thr Val Glu
340 345 350

Glu Pro Ser Asn Pro Glu Ala Ser Ser Ser Thr Ser Val Thr Pro Asp
355 360 365

Val Ser Asp Asn Glu Pro Asp His Tyr Arg Tyr Ser Asp Thr Thr Asp
370 375 380

Ser Asp Pro Glu Asn Glu Pro Phe Asp Glu Asp Gln His Thr Gln Ile
385 390 395 400

Thr Lys Val

<210> 161
<211> 336
<212> PRT
<213> Human

<400> 161

Met Leu Gln Ser Leu Ala Gly Ser Ser Cys Val Arg Leu Val Glu Arg
1 5 10 15

His Arg Ser Ala Trp Cys Phe Gly Phe Leu Val Leu Gly Tyr Leu Leu
20 25 30

Tyr Leu Val Phe Gly Ala Val Val Phe Ser Ser Val Glu Leu Pro Tyr
35 40 45

Glu Asp Leu Leu Arg Gln Glu Leu Arg Lys Leu Lys Arg Arg Phe Leu
50 55 60

Glu Glu His Glu Cys Leu Ser Glu Gln Gln Leu Glu Gln Phe Leu Gly
65 70 75 80

Arg Val Leu Glu Ala Ser Asn Tyr Gly Val Ser Val Leu Ser Asn Ala
85 90 95

Ser Gly Asn Trp Asn Trp Asp Phe Thr Ser Ala Leu Phe Phe Ala Ser
100 105 110

Thr Val Leu Ser Thr Thr Gly Tyr Gly His Thr Val Pro Leu Ser Asp
115 120 125

Gly Gly Lys Ala Phe Cys Ile Ile Tyr Ser Val Ile Gly Ile Pro Phe
130 135 140

Thr Leu Leu Phe Leu Thr Ala Val Val Gln Arg Ile Thr Val His Val
145 150 155 160

Thr Arg Arg Pro Val Leu Tyr Phe His Ile Arg Trp Gly Phe Ser Lys
165 170 175

Gln Val Val Ala Ile Val His Ala Val Leu Leu Gly Phe Val Thr Val
180 185 190

Ser Cys Phe Phe Phe Ile Pro Ala Ala Val Phe Ser Val Leu Glu Asp
195 200 205

Asp Trp Asn Phe Leu Glu Ser Phe Tyr Phe Cys Phe Ile Ser Leu Ser
210 215 220

Thr Ile Gly Leu Gly Asp Tyr Val Pro Gly Glu Gly Tyr Asn Gln Lys
225 230 235 240

Phe Arg Glu Leu Tyr Lys Ile Gly Ile Thr Cys Tyr Leu Leu Leu Gly
245 250 255

Leu Ile Ala Met Leu Val Val Leu Glu Thr Phe Cys Glu Leu His Glu
260 265 270

Leu Lys Lys Phe Arg Lys Met Phe Tyr Val Lys Lys Asp Lys Asp Glu
275 280 285

Asp Gln Val His Ile Ile Glu His Asp Gln Leu Ser Phe Ser Ser Ile

290 295 300

Thr Asp Gln Ala Ala Gly Met Lys Glu Asp Gln Lys Gln Asn Glu Pro
305 310 315 320

Phe Val Ala Thr Gln Ser Ser Ala Cys Val Asp Gly Pro Ala Asn His
325 330 335

<210> 162
<211> 604
<212> PRT
<213> Human

<400> 162

Met Leu Ala Arg Ala Leu Leu Leu Cys Ala Val Leu Ala Leu Ser His
1 5 10 15

Thr Ala Asn Pro Cys Cys Ser His Pro Cys Gln Asn Arg Gly Val Cys
20 25 30

Met Ser Val Gly Phe Asp Gln Tyr Lys Cys Asp Cys Thr Arg Thr Gly
35 40 45

Phe Tyr Gly Glu Asn Cys Ser Thr Pro Glu Phe Leu Thr Arg Ile Lys
50 55 60

Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His
65 70 75 80

Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn
85 90 95

Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser
100 105 110

Pro Pro Thr Tyr Asn Ala Asp Tyr Gly Tyr Lys Ser Trp Glu Ala Phe
115 120 125

Ser Asn Leu Ser Tyr Tyr Thr Arg Ala Leu Pro Pro Val Pro Asp Asp
130 135 140

Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser
145 150 155 160

Asn Glu Ile Val Glu Lys Leu Leu Leu Arg Arg Lys Phe Ile Pro Asp

165 170 175

Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr
180 185 190

His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn
195 200 205

Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu
210 215 220

Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr
225 230 235 240

Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln
245 250 255

Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala
260 265 270

Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala
275 280 285

Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln
290 295 300

Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu
305 310 315 320

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln
325 330 335

His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu
340 345 350

Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn
355 360 365

Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His
370 375 380

Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu
385 390 395 400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile
405 410 415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys
420 425 430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser
435 440 445

Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe
450 455 460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu
465 470 475 480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu
485 490 495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly
500 505 510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro
515 520 525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile
530 535 540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly
545 550 555 560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr
565 570 575

Val Thr Ile Asn Ala Ser Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn
580 585 590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu
595 600

<210> 163
<211> 117
<212> PRT
<213> Human

<400> 163

Met Arg Ala Ser Ser Phe Leu Ile Val Val Val Phe Leu Ile Ala Gly
1 5 10 15

Thr Leu Val Leu Glu Ala Ala Val Thr Gly Val Pro Val Lys Gly Gln
20 25 30

Asp Thr Val Lys Gly Arg Val Pro Phe Asn Gly Gln Asp Pro Val Lys
35 40 45

Gly Gln Val Ser Val Lys Gly Gln Asp Lys Val Lys Ala Gln Glu Pro
50 55 60

Val Lys Gly Pro Val Ser Thr Lys Pro Gly Ser Cys Pro Ile Ile Leu
65 70 75 80

Ile Arg Cys Ala Met Leu Asn Pro Pro Asn Arg Cys Leu Lys Asp Thr
85 90 95

Asp Cys Pro Gly Ile Lys Lys Cys Cys Glu Gly Ser Cys Gly Met Ala
100 105 110

Cys Phe Val Pro Gln
115

<210> 164
<211> 464
<212> PRT
<213> Human

<400> 164

Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp
1 5 10 15

Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
20 25 30

Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
35 40 45

Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln
50 55 60

Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn
65 70 75 80

Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu
85 90 95

Phe Asp Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser
100 105 110

Asn Ser Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp
115 120 125

Asp Tyr Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro
130 135 140

Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser
145 150 155 160

His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu
165 170 175

His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu
180 185 190

Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro
195 200 205

Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe
210 215 220

Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile
225 230 235 240

Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu
245 250 255

Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg
260 265 270

Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp
275 280 285

Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg
290 295 300

Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu
305 310 315 320

Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln
325 330 335

Ile Leu Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu
340 345 350

Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met
355 360 365

Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro
370 375 380

Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe
385 390 395 400

Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu
405 410 415

Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala
420 425 430

Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr
435 440 445

Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
450 455 460

<210> 165
<211> 156
<212> PRT
<213> Human

<400> 165

Met Ala Leu Glu Lys Ser Leu Val Arg Leu Leu Leu Leu Val Leu Ile
1 5 10 15

Leu Leu Val Leu Gly Trp Val Gln Pro Ser Leu Gly Lys Glu Ser Arg
20 25 30

Ala Lys Lys Phe Gln Arg Gln His Met Asp Ser Asp Ser Ser Pro Ser
35 40 45

Ser Ser Ser Thr Tyr Cys Asn Gln Met Met Arg Arg Arg Asn Met Thr
50 55 60

Gln Gly Arg Cys Lys Pro Val Asn Thr Phe Val His Glu Pro Leu Val
65 70 75 80

Asp Val Gln Asn Val Cys Phe Gln Glu Lys Val Thr Cys Lys Asn Gly
85 90 95

Gln Gly Asn Cys Tyr Lys Ser Asn Ser Ser Met His Ile Thr Asp Cys
100 105 110

Arg Leu Thr Asn Gly Ser Arg Tyr Pro Asn Cys Ala Tyr Arg Thr Ser
115 120 125

Pro Lys Glu Arg His Ile Ile Val Ala Cys Glu Gly Ser Pro Tyr Val
130 135 140

Pro Val His Phe Asp Ala Ser Val Glu Asp Ser Thr
145 150 155

<210> 166
<211> 375
<212> PRT
<213> Human

<400> 166

Met Asp Ala Leu Gln Leu Ala Asn Ser Ala Phe Ala Val Asp Leu Phe
1 5 10 15

Lys Gln Leu Cys Glu Lys Glu Pro Leu Gly Asn Val Leu Phe Ser Pro
20 25 30

Ile Cys Leu Ser Thr Ser Leu Ser Leu Ala Gln Val Gly Ala Lys Gly
35 40 45

Asp Thr Ala Asn Glu Ile Gly Gln Val Leu His Phe Glu Asn Val Lys
50 55 60

Asp Ile Pro Phe Gly Phe Gln Thr Val Thr Ser Asp Val Asn Lys Leu
65 70 75 80

Ser Ser Phe Tyr Ser Leu Lys Leu Ile Lys Arg Leu Tyr Val Asp Lys
85 90 95

Ser Leu Asn Leu Ser Thr Glu Phe Ile Ser Ser Thr Lys Arg Pro Tyr
100 105 110

Ala Lys Glu Leu Glu Thr Val Asp Phe Lys Asp Lys Leu Glu Glu Thr
115 120 125

Lys Gly Gln Ile Asn Asn Ser Ile Lys Asp Leu Thr Asp Gly His Phe
130 135 140

Glu Asn Ile Leu Ala Asp Asn Ser Val Asn Asp Gln Thr Lys Ile Leu
145 150 155 160

Val Val Asn Ala Ala Tyr Phe Val Gly Lys Trp Met Lys Lys Phe Pro
165 170 175

Glu Ser Glu Thr Lys Glu Cys Pro Phe Arg Leu Asn Lys Thr Asp Thr
180 185 190

Lys Pro Val Gln Met Met Asn Met Glu Ala Thr Phe Cys Met Gly Asn
195 200 205

Ile Asp Ser Ile Asn Cys Lys Ile Ile Glu Leu Pro Phe Gln Asn Lys
210 215 220

His Leu Ser Met Phe Ile Leu Leu Pro Lys Asp Val Glu Asp Glu Ser
225 230 235 240

Thr Gly Leu Glu Lys Ile Glu Lys Gln Leu Asn Ser Glu Ser Leu Ser
245 250 255

Gln Trp Thr Asn Pro Ser Thr Met Ala Asn Ala Lys Val Lys Leu Ser
260 265 270

Ile Pro Lys Phe Lys Val Glu Lys Met Ile Asp Pro Lys Ala Cys Leu
275 280 285

Glu Asn Leu Gly Leu Lys His Ile Phe Ser Glu Asp Thr Ser Asp Phe
290 295 300

Ser Gly Met Ser Glu Thr Lys Gly Val Ala Leu Ser Asn Val Ile His
305 310 315 320

Lys Val Cys Leu Glu Ile Thr Glu Asp Gly Gly Asp Ser Ile Glu Val
325 330 335

Pro Gly Ala Arg Ile Leu Gln His Lys Asp Glu Leu Asn Ala Asp His
340 345 350

Pro Phe Ile Tyr Ile Ile Arg His Asn Lys Thr Arg Asn Ile Ile Phe
355 360 365

Phe Gly Lys Phe Cys Ser Pro
370 375

<210> 167
<211> 240
<212> PRT
<213> Human

<400> 167

Met Leu Ala Leu Leu Cys Ser Cys Leu Leu Leu Ala Ala Gly Ala Ser
1 5 10 15

Asp Ala Trp Thr Gly Glu Asp Ser Ala Glu Pro Asn Ser Asp Ser Ala
20 25 30

Glu Trp Ile Arg Asp Met Tyr Ala Lys Val Thr Glu Ile Trp Gln Glu
35 40 45

Val Met Gln Arg Arg Asp Asp Asp Gly Thr Leu His Ala Ala Cys Gln
50 55 60

Val Gln Pro Ser Ala Thr Leu Asp Ala Ala Gln Pro Arg Val Thr Gly
65 70 75 80

Val Val Leu Phe Arg Gln Leu Ala Pro Arg Ala Lys Leu Asp Ala Phe
85 90 95

Phe Ala Leu Glu Gly Phe Pro Thr Glu Pro Asn Ser Ser Ser Arg Ala
100 105 110

Ile His Val His Gln Phe Gly Asp Leu Ser Gln Gly Cys Glu Ser Thr
115 120 125

Gly Pro His Tyr Asn Pro Leu Ala Val Pro His Pro Gln His Pro Gly
130 135 140

Asp Phe Gly Asn Phe Ala Val Arg Asp Gly Ser Leu Trp Arg Tyr Arg
145 150 155 160

Ala Gly Leu Ala Ala Ser Leu Ala Gly Pro His Ser Ile Val Gly Arg
165 170 175

Ala Val Val Val His Ala Gly Glu Asp Asp Leu Gly Arg Gly Gly Asn
180 185 190

Gln Ala Ser Val Glu Asn Gly Asn Ala Gly Arg Arg Leu Ala Cys Cys
195 200 205

Val Val Gly Val Cys Gly Pro Gly Leu Trp Glu Arg Gln Ala Arg Glu
210 215 220

His Ser Glu Arg Lys Lys Arg Arg Arg Glu Ser Glu Cys Lys Ala Ala
225 230 235 240

<210> 168
<211> 283
<212> PRT
<213> Human

<400> 168

Met Glu Pro Pro Gly Asp Trp Gly Pro Pro Pro Trp Arg Ser Thr Pro
1 5 10 15

Arg Thr Asp Val Leu Arg Leu Val Leu Tyr Leu Thr Phe Leu Gly Ala
20 25 30

Pro Cys Tyr Ala Pro Ala Leu Pro Ser Cys Lys Glu Asp Glu Tyr Pro
35 40 45

Val Gly Ser Glu Cys Cys Pro Lys Cys Ser Pro Gly Tyr Arg Val Lys
50 55 60

Glu Ala Cys Gly Glu Leu Thr Gly Thr Val Cys Glu Pro Cys Pro Pro
65 70 75 80

Gly Thr Tyr Ile Ala His Leu Asn Gly Leu Ser Lys Cys Leu Gln Cys
85 90 95

Gln Met Cys Asp Pro Ala Met Gly Leu Arg Ala Ser Arg Asn Cys Ser
100 105 110

Arg Thr Glu Asn Ala Val Cys Gly Cys Ser Pro Gly His Phe Cys Ile
115 120 125

Val Gln Asp Gly Asp His Cys Ala Ala Cys Arg Ala Tyr Ala Thr Ser
130 135 140

Ser Pro Gly Gln Arg Val Gln Lys Gly Gly Thr Glu Ser Gln Asp Thr
145 150 155 160

Leu Cys Gln Asn Cys Pro Pro Gly Thr Phe Ser Pro Asn Gly Thr Leu
165 170 175

Glu Glu Cys Gln His Gln Thr Lys Cys Ser Trp Leu Val Thr Lys Ala
180 185 190

Gly Ala Gly Thr Ser Ser Ser His Trp Val Trp Trp Phe Leu Ser Gly
195 200 205

Ser Leu Val Ile Val Ile Val Cys Ser Thr Val Gly Leu Ile Ile Cys
210 215 220

Val Lys Arg Arg Lys Pro Arg Gly Asp Val Val Lys Val Ile Val Ser
225 230 235 240

Val Gln Arg Lys Arg Gln Glu Ala Glu Gly Glu Ala Thr Val Ile Glu
245 250 255

Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu Thr
260 265 270

Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
275 280

<210> 169
<211> 335
<212> PRT
<213> Human

<400> 169

Met Leu Gly Ile Trp Thr Leu Leu Pro Leu Val Leu Thr Ser Val Ala
1 5 10 15

Arg Leu Ser Ser Lys Ser Val Asn Ala Gln Val Thr Asp Ile Asn Ser
20 25 30

Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn
35 40 45

Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro
50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro
65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His
85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly
100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg
115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp
130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr
145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp
165 170 175

Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg
180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly
195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu
210 215 220

Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met
225 230 235 240

Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu
245 250 255

Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu
260 265 270

Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys
275 280 285

Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys

290 295 300

Thr Leu Ala Glu Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser
305 310 315 320

Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
325 330 335

<210> 170
<211> 207
<212> PRT
<213> Human

<400> 170

Met Asn Val Ala Arg Phe Leu Val Glu Lys His Thr Leu His Val Ile
1 5 10 15

Ile Asp Phe Ile Leu Ser Lys Val Ser Asn Gln Gln Ser Asn Leu Ala
20 25 30

Gln His Gln Arg Val Tyr Thr Gly Glu Lys Pro Tyr Lys Cys Asn Glu
35 40 45

Trp Gly Lys Ala Leu Ser Gly Lys Ser Ser Leu Phe Tyr His Gln Ala
50 55 60

Ile His Gly Val Gly Lys Leu Cys Lys Cys Asn Asp Cys His Lys Val
65 70 75 80

Phe Ser Asn Ala Thr Thr Ile Ala Asn His Trp Arg Ile His Asn Glu
85 90 95

Asp Arg Ser Tyr Lys Cys Asn Lys Cys Gly Lys Ile Phe Arg His Arg
100 105 110

Ser Tyr Leu Ala Val Tyr Gln Arg Thr His Thr Gly Glu Lys Pro Tyr
115 120 125

Lys Tyr His Asp Cys Gly Lys Val Phe Ser Gln Ala Ser Ser Tyr Ala
130 135 140

Lys His Arg Arg Ile His Thr Gly Glu Lys Pro His Lys Cys Asp Asp
145 150 155 160

Cys Gly Lys Val Leu Thr Ser Arg Ser His Leu Ile Arg His Gln Arg

165 170 175

Ile His Thr Gly Gln Lys Ser Tyr Lys Cys Leu Lys Cys Gly Lys Val
180 185 190

Phe Ser Leu Trp Ala Leu His Ala Glu His Gln Lys Ile His Phe
195 200 205

<210> 171
<211> 158
<212> PRT
<213> Human

<400> 171

Met Ala Ser Arg Ser Met Arg Leu Leu Leu Leu Leu Ser Cys Leu Ala
1 5 10 15

Lys Thr Gly Val Leu Gly Asp Ile Ile Met Arg Pro Ser Cys Ala Pro
20 25 30

Gly Trp Phe Tyr His Lys Ser Asn Cys Tyr Gly Tyr Phe Arg Lys Leu
35 40 45

Arg Asn Trp Ser Asp Ala Glu Leu Glu Cys Gln Ser Tyr Gly Asn Gly
50 55 60

Ala His Leu Ala Ser Ile Leu Ser Leu Lys Glu Ala Ser Thr Ile Ala
65 70 75 80

Glu Tyr Ile Ser Gly Tyr Gln Arg Ser Gln Pro Ile Trp Ile Gly Leu
85 90 95

His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met
100 105 110

Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His
115 120 125

Cys Ala Glu Met Ser Ser Asn Asn Asn Phe Leu Thr Trp Ser Ser Asn
130 135 140

Glu Cys Asn Lys Arg Gln His Phe Leu Cys Lys Tyr Arg Pro
145 150 155

<210> 172

<211> 432
<212> PRT
<213> Human

<400> 172

Met Gly Pro Ala Gly Ser Leu Leu Gly Ser Gly Gln Met Gln Ile Thr
1   5   10   15

Leu Trp Gly Ser Leu Ala Ala Val Ala Ile Phe Phe Val Ile Thr Phe
            20   25   30

Leu Ile Phe Pro Cys Ser Ser Cys Asp Arg Glu Lys Lys Pro Arg Gln
        35   40   45

His Ser Gly Asp His Glu Asn Leu Met Asn Val Pro Ser Asp Lys Glu
    50   55   60

Met Phe Ser Arg Ser Val Thr Ser Leu Ala Thr Asp Ala Pro Ala Ser
65   70   75   80

Ser Glu Gln Asn Gly Ala Leu Thr Asn Gly Asp Ile Leu Ser Glu Asp
                85   90   95

Ser Thr Leu Thr Cys Met Gln His Tyr Glu Glu Val Gln Thr Ser Ala
            100   105   110

Ser Asp Leu Leu Asp Ser Gln Asp Ser Thr Gly Lys Pro Lys Cys His
        115   120   125

Gln Ser Arg Glu Leu Pro Arg Ile Pro Pro Glu Ser Ala Val Asp Thr
    130   135   140

Met Leu Thr Ala Arg Ser Val Asp Gly Asp Gln Gly Leu Gly Met Glu
145   150   155   160

Gly Pro Tyr Glu Val Leu Lys Asp Ser Ser Ser Gln Glu Asn Met Val
                165   170   175

Glu Asp Cys Leu Tyr Glu Thr Val Lys Glu Ile Lys Glu Val Ala Ala
            180   185   190

Ala Ala His Leu Glu Lys Gly His Ser Gly Lys Ala Lys Ser Thr Ser
        195   200   205

Ala Ser Lys Glu Leu Pro Gly Pro Gln Thr Glu Gly Lys Ala Glu Phe

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    210                 215                 220

Ala Glu Tyr Ala Ser Val Asp Arg Asn Lys Lys Cys Arg Gln Ser Val
225                 230                 235                 240

Asn Val Glu Ser Ile Leu Gly Asn Ser Cys Asp Pro Glu Glu Glu Ala
                245                 250                 255

Pro Pro Pro Val Pro Val Lys Leu Leu Asp Glu Asn Glu Asn Leu Gln
            260                 265                 270

Glu Lys Glu Gly Gly Glu Ala Glu Glu Ser Ala Thr Asp Thr Thr Ser
        275                 280                 285

Glu Thr Asn Lys Arg Phe Ser Ser Leu Ser Tyr Lys Ser Arg Glu Glu
    290                 295                 300

Asp Pro Thr Leu Thr Glu Glu Glu Ile Ser Ala Met Tyr Ser Ser Val
305                 310                 315                 320

Asn Lys Pro Gly Gln Leu Val Asn Lys Ser Gly Gln Ser Leu Thr Val
                325                 330                 335

Pro Glu Ser Thr Tyr Thr Ser Ile Gln Gly Asp Pro Gln Arg Ser Pro
            340                 345                 350

Ser Ser Cys Asn Asp Leu Tyr Ala Thr Val Lys Asp Phe Glu Lys Thr
        355                 360                 365

Pro Asn Ser Thr Leu Pro Pro Ala Gly Arg Pro Ser Glu Glu Pro Glu
    370                 375                 380

Pro Asp Tyr Glu Ala Ile Gln Thr Leu Asn Arg Glu Glu Glu Lys Ala
385                 390                 395                 400

Thr Leu Gly Thr Asn Gly His His Gly Leu Val Pro Lys Glu Asn Asp
                405                 410                 415

Tyr Glu Ser Ile Ser Asp Leu Gln Gln Gly Arg Asp Ile Thr Arg Leu
            420                 425                 430
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<210> 173
<211> 174
<212> PRT
<213> Human

<400> 173

Lys Pro Phe Arg Cys Glu Asn Cys Asn Glu Arg Phe Gln Tyr Lys Tyr
1 5 10 15

Gln Leu Arg Ser His Met Ser Ile His Ile Gly His Lys Gln Phe Met
20 25 30

Cys Gln Trp Cys Gly Lys Asp Phe Asn Met Lys Gln Tyr Phe Asp Glu
35 40 45

His Met Lys Thr His Thr Gly Glu Lys Pro Tyr Ile Cys Glu Ile Cys
50 55 60

Gly Lys Ser Phe Thr Ser Arg Pro Asn Met Lys Arg His Arg Arg Thr
65 70 75 80

His Thr Gly Glu Lys Pro Tyr Pro Cys Asp Val Cys Gly Gln Arg Phe
85 90 95

Arg Phe Ser Asn Met Leu Lys Ala His Lys Glu Lys Cys Phe Arg Val
100 105 110

Ser His Thr Leu Ala Gly Asp Gly Val Pro Ala Ala Pro Gly Leu Pro
115 120 125

Pro Thr Gln Pro Gln Ala His Ala Leu Pro Leu Leu Pro Gly Leu Pro
130 135 140

Gln Thr Leu Pro Pro Pro Pro His Leu Pro Pro Pro Pro Pro Leu Phe
145 150 155 160

Pro Thr Thr Ala Ser Pro Gly Gly Arg Met Asn Ala Asn Asn
165 170

<210> 174
<211> 917
<212> PRT
<213> Human

<400> 174

Ala Ser Pro Arg Gly Thr Glu Ala Ser Pro Pro Gln Asn Asn Ser Gly
1 5 10 15

Ser Ser Ser Pro Val Phe Thr Phe Arg His Pro Leu Leu Ser Ser Gly

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            20                  25                  30

Gly Pro Gln Ser Pro Leu Arg Gly Ser Thr Gly Ser Leu Lys Ser Ser
        35                  40                  45

Pro Ser Met Ser His Met Glu Ala Leu Gly Lys Ala Trp Asn Arg Gln
    50                  55                  60

Leu Ser Arg Pro Leu Ser Gln Ala Val Ser Phe Ser Thr Pro Phe Gly
65                  70                  75                  80

Leu Asp Ser Asp Val Asp Val Val Met Gly Asp Pro Val Leu Leu Arg
                85                  90                  95

Ser Val Ser Ser Asp Ser Leu Gly Pro Pro Arg Pro Ala Pro Ala Arg
            100                 105                 110

Thr Pro Thr Gln Pro Pro Pro Glu Pro Gly Asp Leu Pro Thr Ile Glu
        115                 120                 125

Glu Ala Leu Gln Ile Ile His Ser Ala Glu Pro Arg Leu Leu Pro Asp
    130                 135                 140

Gly Ala Ala Asp Gly Ser Phe Tyr Leu His Ser Pro Glu Gly Pro Ser
145                 150                 155                 160

Lys Pro Ser Leu Ala Ser Pro Tyr Leu Pro Glu Gly Thr Ser Lys Pro
                165                 170                 175

Leu Ser Asp Arg Pro Thr Lys Ala Pro Val Tyr Met Pro His Pro Glu
            180                 185                 190

Thr Pro Ser Lys Pro Ser Pro Cys Leu Val Gly Glu Ala Ser Lys Pro
        195                 200                 205

Pro Ala Pro Ser Glu Gly Ser Pro Lys Ala Val Ala Ser Ser Pro Ala
    210                 215                 220

Ala Thr Asn Ser Glu Val Lys Met Thr Ser Phe Ala Glu Arg Lys Lys
225                 230                 235                 240

Gln Leu Val Lys Ala Glu Ala Glu Ala Gly Ala Gly Ser Pro Thr Ser
                245                 250                 255
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Thr Pro Ala Pro Pro Glu Ala Leu Ser Ser Glu Met Ser Glu Leu Ser
260 265 270

Ala Arg Leu Glu Glu Lys Arg Arg Ala Ile Glu Ala Gln Lys Arg Arg
275 280 285

Ile Glu Ala Ile Phe Ala Lys His Arg Gln Arg Leu Gly Lys Ser Ala
290 295 300

Phe Leu Gln Val Gln Pro Arg Glu Ala Ser Gly Glu Ala Glu Ala Glu
305 310 315 320

Ala Glu Glu Ala Asp Ser Gly Pro Val Pro Gly Gly Glu Arg Pro Ala
325 330 335

Gly Glu Gly Gln Gly Glu Pro Thr Ser Arg Pro Lys Ala Val Thr Phe
340 345 350

Ser Pro Asp Leu Gly Pro Val Pro His Glu Gly Leu Gly Glu Tyr Asn
355 360 365

Arg Ala Val Ser Lys Leu Ser Ala Ala Leu Ser Ser Leu Gln Arg Asp
370 375 380

Met Gln Arg Leu Thr Asp Gln Gln Gln Arg Leu Leu Ala Pro Pro Glu
385 390 395 400

Ala Pro Gly Ser Ala Pro Pro Pro Ala Ala Trp Val Ile Pro Gly Pro
405 410 415

Thr Thr Gly Pro Lys Ala Ala Ser Pro Ser Pro Ala Arg Arg Val Pro
420 425 430

Ala Thr Arg Arg Ser Pro Gly Pro Gly Pro Ser Gln Ser Pro Arg Ser
435 440 445

Pro Lys His Thr Arg Pro Ala Glu Leu Arg Leu Ala Pro Leu Thr Arg
450 455 460

Val Leu Thr Pro Pro His Asp Val Asp Ser Leu Pro His Leu Arg Lys
465 470 475 480

Phe Ser Pro Ser Gln Val Pro Val Gln Thr Arg Ser Ser Ile Leu Leu
485 490 495

Ala Glu Glu Thr Pro Pro Glu Glu Pro Ala Ala Arg Pro Gly Leu Ile
500 505 510

Glu Ile Pro Leu Gly Ser Leu Ala Asp Pro Ala Ala Glu Asp Glu Gly
515 520 525

Asp Gly Ser Pro Ala Gly Ala Glu Asp Ser Leu Glu Glu Glu Ala Ser
530 535 540

Ser Glu Gly Glu Pro Arg Val Gly Leu Gly Phe Phe Tyr Lys Asp Glu
545 550 555 560

Asp Lys Pro Glu Asp Glu Met Ala Gln Lys Arg Ala Ser Leu Leu Glu
565 570 575

Arg Gln Gln Arg Arg Ala Glu Glu Ala Arg Arg Arg Lys Gln Trp Gln
580 585 590

Glu Val Glu Lys Glu Gln Arg Arg Glu Glu Ala Ala Arg Leu Ala Gln
595 600 605

Glu Glu Ala Pro Gly Pro Ala Pro Leu Val Ser Ala Val Pro Met Ala
610 615 620

Thr Pro Ala Pro Ala Ala Arg Ala Pro Ala Glu Glu Glu Val Gly Pro
625 630 635 640

Arg Lys Gly Asp Phe Thr Arg Gln Glu Tyr Glu Arg Arg Ala Gln Leu
645 650 655

Lys Leu Met Asp Asp Leu Asp Lys Val Leu Arg Pro Arg Ala Ala Gly
660 665 670

Ser Gly Gly Pro Gly Arg Gly Gly Arg Arg Ala Thr Arg Pro Arg Ser
675 680 685

Gly Cys Cys Asp Asp Ser Ala Leu Ala Arg Ser Pro Ala Arg Gly Leu
690 695 700

Leu Gly Ser Arg Leu Ser Lys Ile Tyr Ser Gln Ser Thr Leu Ser Leu
705 710 715 720

Ser Thr Val Ala Asn Glu Ala His Asn Asn Leu Gly Val Lys Arg Pro
725 730 735

Thr Ser Arg Ala Pro Ser Pro Ser Gly Leu Met Ser Pro Ser Arg Leu
740 745 750

Pro Gly Ser Arg Glu Arg Asp Trp Glu Asn Gly Ser Asn Ala Ser Ser
755 760 765

Pro Ala Ser Val Pro Glu Tyr Thr Gly Pro Arg Leu Tyr Lys Glu Pro
770 775 780

Ser Ala Lys Ser Asn Lys Phe Ile Ile His Asn Ala Leu Ser His Cys
785 790 795 800

Cys Leu Ala Gly Lys Val Asn Glu Pro Gln Lys Asn Arg Ile Leu Glu
805 810 815

Glu Ile Glu Lys Ser Lys Ala Asn His Phe Leu Ile Leu Phe Arg Asp
820 825 830

Ser Ser Cys Gln Phe Arg Ala Leu Tyr Thr Leu Ser Gly Glu Thr Glu
835 840 845

Glu Leu Ser Arg Leu Ala Gly Tyr Gly Pro Arg Thr Val Thr Pro Ala
850 855 860

Met Val Glu Gly Ile Tyr Lys Tyr Asn Ser Asp Arg Lys Arg Phe Thr
865 870 875 880

Gln Ile Pro Ala Lys Thr Met Ser Met Ser Val Asp Ala Phe Thr Ile
885 890 895

Gln Gly His Leu Trp Gln Gly Lys Lys Pro Thr Thr Pro Lys Lys Gly
900 905 910

Gly Gly Thr Pro Lys
915

<210> 175
<211> 600
<212> PRT
<213> Human

<400> 175

Met Arg Ser Cys Leu Trp Arg Cys Arg His Leu Ser Gln Gly Val Gln
1 5 10 15

Trp Ser Leu Leu Leu Ala Val Leu Val Phe Phe Leu Phe Ala Leu Pro
20 25 30

Ser Phe Ile Lys Glu Pro Gln Thr Lys Pro Ser Arg His Gln Arg Thr
35 40 45

Glu Asn Ile Lys Glu Arg Ser Leu Gln Ser Leu Ala Lys Pro Lys Ser
50 55 60

Gln Ala Pro Thr Arg Ala Arg Arg Thr Thr Ile Tyr Ala Glu Pro Val
65 70 75 80

Pro Glu Asn Asn Ala Leu Asn Thr Gln Thr Gln Pro Lys Ala His Thr
85 90 95

Thr Gly Asp Arg Gly Lys Glu Ala Asn Gln Ala Pro Pro Glu Glu Gln
100 105 110

Asp Lys Val Pro His Thr Ala Gln Arg Ala Ala Trp Lys Ser Pro Glu
115 120 125

Lys Glu Lys Thr Met Val Asn Thr Leu Ser Pro Arg Gly Gln Asp Ala
130 135 140

Gly Met Ala Ser Gly Arg Thr Glu Ala Gln Ser Trp Lys Ser Gln Asp
145 150 155 160

Thr Lys Thr Thr Gln Gly Asn Gly Gly Gln Thr Arg Lys Leu Thr Ala
165 170 175

Ser Arg Thr Val Ser Glu Lys His Gln Gly Lys Ala Ala Thr Thr Ala
180 185 190

Lys Thr Leu Ile Pro Lys Ser Gln His Arg Met Leu Ala Pro Thr Gly
195 200 205

Ala Val Ser Thr Arg Thr Arg Gln Lys Gly Val Thr Thr Ala Val Ile
210 215 220

Pro Pro Lys Glu Lys Lys Pro Gln Ala Thr Pro Pro Pro Ala Pro Phe
225 230 235 240

Gln Ser Pro Thr Thr Gln Arg Asn Gln Arg Leu Lys Ala Ala Asn Phe

245 250 255

Lys Ser Glu Pro Arg Trp Asp Phe Glu Glu Lys Tyr Ser Phe Glu Ile
260 265 270

Gly Gly Leu Gln Thr Thr Cys Pro Asp Ser Val Lys Ile Lys Ala Ser
275 280 285

Lys Ser Leu Trp Leu Gln Lys Leu Phe Leu Pro Asn Leu Thr Leu Phe
290 295 300

Leu Asp Ser Arg His Phe Asn Gln Ser Glu Trp Asp Arg Leu Glu His
305 310 315 320

Phe Ala Pro Pro Phe Gly Phe Met Glu Leu Asn Tyr Ser Leu Val Gln
325 330 335

Lys Val Val Thr Arg Phe Pro Pro Val Pro Gln Gln Gln Leu Leu Leu
340 345 350

Ala Ser Leu Pro Ala Gly Ser Leu Arg Cys Ile Thr Cys Ala Val Val
355 360 365

Gly Asn Gly Gly Ile Leu Asn Asn Ser His Met Gly Gln Glu Ile Asp
370 375 380

Ser His Asp Tyr Val Phe Arg Leu Ser Gly Ala Leu Ile Lys Gly Tyr
385 390 395 400

Glu Gln Asp Val Gly Thr Arg Thr Ser Phe Tyr Gly Phe Thr Ala Phe
405 410 415

Ser Leu Thr Gln Ser Leu Leu Ile Leu Gly Asn Arg Gly Phe Lys Asn
420 425 430

Val Pro Leu Gly Lys Asp Val Arg Tyr Leu His Phe Leu Glu Gly Thr
435 440 445

Arg Asp Tyr Glu Trp Leu Glu Ala Leu Leu Met Asn Gln Thr Val Met
450 455 460

Ser Lys Asn Leu Phe Trp Phe Arg His Arg Pro Gln Glu Ala Phe Arg
465 470 475 480

Glu Ala Leu His Met Asp Arg Tyr Leu Leu Leu His Pro Asp Phe Leu
485 490 495

Arg Tyr Met Lys Asn Arg Phe Leu Arg Ser Lys Thr Leu Asp Gly Ala
500 505 510

His Trp Arg Ile Tyr Arg Pro Thr Thr Gly Ala Leu Leu Leu Leu Thr
515 520 525

Ala Leu Gln Leu Cys Asp Gln Val Ser Ala Tyr Gly Phe Ile Thr Glu
530 535 540

Gly His Glu Arg Phe Ser Asp His Tyr Tyr Asp Thr Ser Trp Lys Arg
545 550 555 560

Leu Ile Phe Tyr Ile Asn His Asp Phe Lys Leu Glu Arg Glu Val Trp
565 570 575

Lys Arg Leu His Asp Glu Gly Ile Ile Arg Leu Tyr Gln Arg Pro Gly
580 585 590

Pro Gly Thr Ala Lys Ala Lys Asn
595 600

<210> 176
<211> 312
<212> PRT
<213> Human

<400> 176

Met Asp Gly Glu Asn His Ser Val Val Ser Glu Phe Leu Phe Leu Gly
1 5 10 15

Leu Thr His Ser Trp Glu Ile Gln Leu Leu Leu Leu Val Phe Ser Ser
20 25 30

Val Leu Tyr Val Ala Ser Ile Thr Gly Asn Ile Leu Ile Val Phe Ser
35 40 45

Val Thr Thr Asp Pro His Leu His Ser Pro Met Tyr Phe Leu Leu Ala
50 55 60

Ser Leu Ser Phe Ile Asp Leu Gly Ala Cys Ser Val Thr Ser Pro Lys
65 70 75 80

Met Ile Tyr Asp Leu Phe Arg Lys Arg Lys Val Ile Ser Phe Gly Gly
85 90 95

Cys Ile Ala Gln Ile Phe Phe Ile His Val Ile Gly Gly Val Glu Met
100 105 110

Val Leu Leu Ile Ala Met Ala Phe Asp Arg Tyr Val Ala Leu Cys Lys
115 120 125

Pro Leu His Tyr Leu Thr Ile Met Ser Pro Arg Met Cys Leu Ser Phe
130 135 140

Leu Ala Val Ala Trp Thr Leu Gly Val Ser His Ser Leu Phe Gln Leu
145 150 155 160

Ala Phe Leu Val Asn Leu Ala Phe Cys Gly Pro Asn Val Leu Asp Ser
165 170 175

Phe Tyr Cys Asp Leu Pro Arg Leu Leu Arg Leu Ala Cys Thr Asp Thr
180 185 190

Tyr Arg Leu Gln Phe Met Val Thr Val Asn Ser Gly Phe Ile Cys Val
195 200 205

Gly Thr Phe Phe Ile Leu Leu Ile Ser Tyr Val Phe Ile Leu Phe Thr
210 215 220

Val Trp Lys His Ser Ser Gly Gly Ser Ser Lys Ala Leu Ser Thr Leu
225 230 235 240

Ser Ala His Ser Thr Val Val Leu Leu Phe Phe Gly Pro Pro Met Phe
245 250 255

Val Tyr Thr Arg Pro His Pro Asn Ser Gln Met Asp Lys Phe Leu Ala
260 265 270

Ile Phe Asp Ala Val Leu Thr Pro Phe Leu Asn Pro Val Val Tyr Thr
275 280 285

Phe Arg Asn Lys Glu Met Lys Ala Ala Ile Lys Arg Val Cys Lys Gln
290 295 300

Leu Val Ile Tyr Lys Arg Ile Ser
305 310

<210> 177
<211> 114
<212> PRT
<213> Human

<400> 177

Met Ala Leu Glu His Leu Val Val Trp His Val His Ser Glu Asp Gln
1 5 10 15

Ser Phe Val Val Leu Lys Thr Asp Leu Gly Arg Arg Gly Cys Arg Pro
20 25 30

Leu Arg Lys Thr Ala Pro Lys Ala Lys Glu Ala Pro Ala Pro Pro Lys
35 40 45

Ala Glu Ala Lys Val Lys Ala Leu Lys Ala Lys Lys Ala Val Leu Lys
50 55 60

Gly Val Arg Ser His Thr Gln Lys Arg Arg Ser Ala Cys His Ser Pro
65 70 75 80

Ser Gly Gly Pro Arg His Cys Asp Ser Gly Gly Ser Pro Asp Ile Leu
85 90 95

Gly Arg Ala Pro Pro Gly Glu Thr Ser Leu Ala Thr Met Leu Ser Ser
100 105 110

Phe Arg

<210> 178
<211> 430
<212> PRT
<213> Human

<400> 178

Asp Ser Met Thr Phe Glu Asp Ile Ile Val Asp Phe Thr Gln Glu Glu
1 5 10 15

Trp Ala Leu Leu Asp Thr Ser Gln Arg Lys Leu Phe Gln Asp Val Met
20 25 30

Leu Glu Asn Ile Ser His Leu Val Ser Ile Gly Glu Asp Phe Thr Gln
35 40 45

His Ile Ala Leu Thr Gln Asn Val Ile Thr Tyr Met Arg Thr Lys His
50 55 60

Phe Val Ser Lys Lys Phe Gly Lys Ile Phe Ser Asp Trp Leu Ser Phe
65 70 75 80

Asn Gln His Lys Glu Ile His Thr Lys Cys Lys Ser Tyr Gly Ser His
85 90 95

Leu Phe Asp Tyr Ala Phe Ile Gln Asn Ser Ala Leu Arg Pro His Ser
100 105 110

Val Thr His Thr Arg Glu Ile Thr Leu Glu Cys Arg Val Cys Gly Lys
115 120 125

Thr Phe Ser Lys Asn Ser Asn Leu Arg Arg His Glu Met Ile His Thr
130 135 140

Gly Glu Lys Pro His Gly Cys His Leu Cys Gly Lys Ala Phe Thr His
145 150 155 160

Cys Ser Asp Leu Arg Lys His Glu Arg Thr His Thr Gly Glu Lys Pro
165 170 175

Tyr Gly Cys His Leu Cys Gly Lys Ala Phe Ser Lys Ser Ser Asn Leu
180 185 190

Arg Arg His Glu Met Ile His Thr Arg Glu Lys Ala Gln Ile Cys His
195 200 205

Leu Cys Gly Lys Ala Phe Thr His Cys Ser Asp Leu Arg Lys His Glu
210 215 220

Arg Thr His Leu Gly Asp Lys Pro Tyr Gly Cys Leu Leu Cys Gly Lys
225 230 235 240

Ala Phe Ser Lys Cys Ser Tyr Leu Arg Gln His Glu Arg Thr His Asn
245 250 255

Gly Glu Lys Pro Tyr Glu Cys His Leu Cys Gly Lys Ala Phe Ser His
260 265 270

Cys Ser His Leu Arg Gln His Glu Arg Ser His Asn Gly Glu Lys Pro
275 280 285

His Gly Cys His Leu Cys Gly Lys Ala Phe Thr Glu Ser Ser Val Leu
290 295 300

Lys Arg His Glu Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys His
305 310 315 320

Val Cys Gly Lys Ala Phe Thr Glu Ser Ser Asp Leu Arg Arg His Glu
325 330 335

Arg Thr His Thr Gly Glu Lys Pro Tyr Glu Cys His Leu Cys Gly Lys
340 345 350

Ala Phe Asn His Ser Ser Val Leu Arg Arg His Glu Arg Thr His Thr
355 360 365

Gly Glu Lys Pro Tyr Glu Cys Asn Ile Cys Gly Lys Ala Phe Asn Arg
370 375 380

Ser Tyr Asn Phe Arg Leu His Arg Arg Val His Thr Gly Glu Lys Pro
385 390 395 400

Tyr Val Cys Pro Leu Cys Gly Lys Ala Phe Ser Lys Phe Phe Asn Leu
405 410 415

Arg Gln His Glu Arg Thr His Thr Lys Lys Ala Met Asn Met
420 425 430

<210> 179
<211> 15
<212> DNA
<213> Murine

<400> 179
aactatggtg tacac 15

<210> 180
<211> 5
<212> PRT
<213> Murine

<400> 180

Asn Tyr Gly Val His
1 5

<210> 181
<211> 48

<212> DNA
<213> Murine

<400> 181
gtgatatgga gtggtggaaa cacagactat aatacacctt tcacatcc 48

<210> 182
<211> 16
<212> PRT
<213> Murine

<400> 182

Val Ile Trp Ser Gly Gly Asn Thr Asp Tyr Asn Thr Pro Phe Thr Ser
1 5 10 15

<210> 183
<211> 33
<212> DNA
<213> Murine

<400> 183
gccctcacct actatgatta cgagtttgct tac 33

<210> 184
<211> 11
<212> PRT
<213> Murine

<400> 184

Ala Leu Thr Tyr Tyr Asp Tyr Glu Phe Ala Tyr
1 5 10

<210> 185
<211> 33
<212> DNA
<213> Murine

<400> 185
agggccagtc agagtattgg cacaaacata cac 33

<210> 186
<211> 11
<212> PRT
<213> Murine

<400> 186

Arg Ala Ser Gln Ser Ile Gly Thr Asn Ile His
1 5 10

<210> 187

<211> 18
<212> DNA
<213> Murine

<400> 187
gcttctgagt ctatctct 18

<210> 188
<211> 6
<212> PRT
<213> Murine

<400> 188

Ala Ser Glu Ser Ile Ser
1 5

<210> 189
<211> 27
<212> DNA
<213> Murine

<400> 189
caacaaaata ataactggcc aaccacg 27

<210> 190
<211> 9
<212> PRT
<213> Murine

<400> 190

Gln Gln Asn Asn Asn Trp Pro Thr Thr
1 5

<210> 191
<211> 17
<212> DNA
<213> Artificial

<220>
<223> GAPDH oligonucleotide

<400> 191
agccgagcca catcgct 17

<210> 192
<211> 19
<212> DNA
<213> Artificial

<220>
<223> GAPDH oligonucleotide

<400> 192
gtgaccaggc gcccaatac 19

<210> 193
<211> 19
<212> DNA
<213> Artificial

<220>
<223> EGFR oligonucleotide

<400> 193
gcgtctcttg ccggaatgt 19

<210> 194
<211> 21
<212> DNA
<213> Artificial

<220>
<223> EGFR oligonucleotide

<400> 194
agccgaggca gggaatgcgt g 21

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,*

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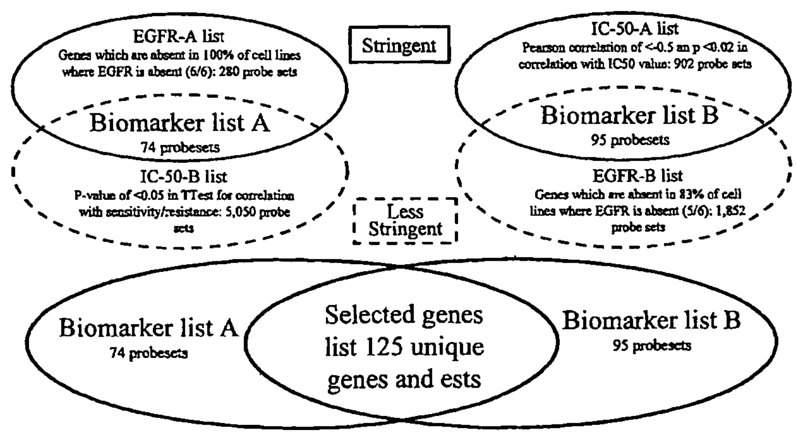
(54) Title: BIOMARKERS AND METHODS FOR DETERMINING SENSITIVITY TO EPIDERMAL GROWTH FACTOR RECEPTOR MODULATORS



(57) Abstract: EGFR biomakers useful in a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises (a) exposing the mammal to the EGFR modulator and (b) measuring in the mammal level of at least one biomaker, wherein a difference in the level in at least one biomaker measured in (b) compared to the level of the biomaker in a mammal that has not been exposed to the EGFR modulator indicates that the mammal will respond therapeutically to the method of treating cancer.

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ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

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